Saethre-Chotzen syndrome

Saethre-Chotzen syndrome is a genetic condition characterized by the premature fusion of certain skull bones (craniosynostosis). This early fusion prevents the skull from growing normally and affects the shape of the head and face.

Most people with Saethre-Chotzen syndrome have prematurely fused skull bones along the coronal suture, the growth line that goes over the head from ear to ear. Other parts of the skull may be malformed as well. These changes can result in an abnormally shaped head, a high forehead, a low frontal hairline, droopy eyelids (ptosis), widely spaced eyes, and a broad nasal bridge. One side of the face may appear noticeably different from the other (facial asymmetry). Most people with Saethre-Chotzen syndrome also have small, unusually shaped ears.

The signs and symptoms of Saethre-Chotzen syndrome vary widely, even among affected individuals in the same family. This condition can cause mild abnormalities of the hands and feet, such as fusion of the skin between the second and third fingers on each hand and a broad or duplicated first (big) toe. Delayed development and learning difficulties have been reported, although most people with this condition are of normal intelligence. Less common signs and symptoms of Saethre-Chotzen syndrome include short stature, abnormalities of the bones of the spine (the vertebra), hearing loss, and heart defects.

Robinow-Sorauf syndrome is a condition with features similar to those of Saethre-Chotzen syndrome, including craniosynostosis and broad or duplicated great toes. It was once considered a separate disorder, but was found to result from mutations in the same gene and is now thought to be a mild variant of Saethre-Chotzen syndrome.

Frequency

Saethre-Chotzen syndrome has an estimated prevalence of 1 in 25,000 to 50,000 people.

Causes

Mutations in the TWIST1 gene cause Saethre-Chotzen syndrome. The TWIST1 gene provides instructions for making a protein that plays an important role in early development. This protein is a transcription factor, which means that it attaches (binds) to specific regions of DNA and helps control the activity of particular genes. The TWIST1 protein is active in cells that give rise to bones, muscles, and other tissues in the head and face. It is also involved in the development of the limbs.

Mutations in the TWIST1 gene prevent one copy of the gene in each cell from making any functional protein. A shortage of the TWIST1 protein affects the development and
maturation of cells in the skull, face, and limbs. These abnormalities underlie the signs and symptoms of Saethre-Chotzen syndrome, including the premature fusion of certain skull bones.

A small number of cases of Saethre-Chotzen syndrome have resulted from a structural chromosomal abnormality, such as a deletion or rearrangement of genetic material, in the region of chromosome 7 that contains the TWIST1 gene. When Saethre-Chotzen syndrome is caused by a chromosomal deletion instead of a mutation within the TWIST1 gene, affected children are much more likely to have intellectual disability, developmental delay, and learning difficulties. These features are typically not seen in classic cases of Saethre-Chotzen syndrome. Researchers believe that a loss of other genes on chromosome 7 may be responsible for these additional features.

**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. In some cases, an affected person inherits the mutation from one affected parent. Other cases may result from new mutations in the gene. These cases occur in people with no history of the disorder in their family.

Some people with a TWIST1 mutation do not have any of the obvious features of Saethre-Chotzen syndrome. These people are still at risk of passing on the gene mutation and may have a child with craniosynostosis and the other typical signs and symptoms of the condition.

**Other Names for This Condition**

- acrocephalosyndactyly III
- Acrocephalosyndactyly, type III
- Acrocephaly, Skull Asymmetry, and Mild Syndactyly
- ACS III
- ACS3
- Chotzen syndrome
- dysostosis craniofacialis with hypertelorism
- SCS
Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Robinow Sorauf syndrome
- Genetic Testing Registry: Saethre-Chotzen syndrome

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Saethre-Chotzen+syndrome%22+OR+%22Acrocephalosyndactylia%22+OR+%22Saethre-Chotzen+Syndrome%22

Other Diagnosis and Management Resources

- GeneReview: Saethre-Chotzen Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1189
- MedlinePlus Encyclopedia: Craniosynostosis
  https://medlineplus.gov/ency/article/001590.htm
- MedlinePlus Encyclopedia: Skull of a Newborn (image)
  https://medlineplus.gov/ency/imagepages/1127.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Craniosynostosis
  https://medlineplus.gov/ency/article/001590.htm
- Encyclopedia: Skull of a Newborn (image)
  https://medlineplus.gov/ency/imagepages/1127.htm
- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html

Genetic and Rare Diseases Information Center

- Saethre-Chotzen syndrome

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Craniosynostosis Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Craniosynostosis-Information-Page
Educational Resources

• Boston Children's Hospital

• Headlines Craniofacial Support (UK)

• Johns Hopkins Collaboration for Craniofacial Development and Disorders
  https://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/pediatric_neurosurgery/conditions/craniosynostosis/

• MalaCards: saethre-chotzen syndrome
  https://www.malacards.org/card/saethre_chotzen_syndrome

• Orphanet: Saethre-Chotzen syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=794

Patient Support and Advocacy Resources

• AmeriFace
  http://www.ameriface.org/

• Children's Craniofacial Association
  https://ccakids.org/

• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/saethre-chotzen-syndrome/

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

Clinical Information from GeneReviews

• Saethre-Chotzen Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1189

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=Acrocephalosyndactyli%5BMAJR%5D%29+AND+%28saethre-chotzen+syndrome%5BWTIAB%5D%29+OR+%28acs3%5BWTIAB%5D%29+OR+%28dysostosis+craniofacialis+with+hypertelorism%5BWTIAB%5D%29+OR+%28chotzen+syndrome%5BWTIAB%5D%29%29+AND+english%5BLa%5D+AND+human%5Bmhm%5D+AND+22last+3600+days%22%5Bdp%5D
Catalog of Genes and Diseases from OMIM

- ROBINOW-SORAUF SYNDROME
  http://omim.org/entry/180750
- SAETHRE-CHOTZEN SYNDROME
  http://omim.org/entry/101400

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14513358
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12791045
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12116251
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