Congenital fibrosis of the extraocular muscles

Congenital fibrosis of the extraocular muscles is a disorder that affects the muscles that surround the eyes. These muscles control eye movement and the position of the eyes (for example, looking straight ahead). Congenital fibrosis of the extraocular muscles prevents the normal development and function of these muscles. As a result, affected individuals are unable to move their eyes normally. Most people with this condition have difficulty looking upward, and their side-to-side eye movement may also be limited. The eyes may be misaligned such that they look in different directions (strabismus). Instead of moving their eyes, affected individuals may need to turn their head to track moving objects. Additionally, many people with congenital fibrosis of the extraocular muscles have droopy eyelids (ptosis), which further limits their vision.

Researchers have identified at least four forms of congenital fibrosis of the extraocular muscles, designated CFEOM1, CFEOM2, CFEOM3, and Tukel syndrome. The specific problems with eye movement vary among the types. Tukel syndrome is characterized by missing fingers (oligodactyly) and other hand abnormalities in addition to problems with eye movement.

Frequency

CFEOM1 is the most common form of congenital fibrosis of the extraocular muscles, affecting at least 1 in 230,000 people. CFEOM1 and CFEOM3 have been reported worldwide, whereas CFEOM2 has been seen in only a few families of Turkish, Saudi Arabian, and Iranian descent. Tukel syndrome appears to be very rare; it has been diagnosed in only one large Turkish family.

Causes

CFEOM1 and rare cases of CFEOM3 result from mutations in the *KIF21A* gene. This gene provides instructions for making a protein called a kinesin, which is essential for the transport of materials within cells. Researchers believe that this protein plays an important role in the normal development and function of nerves in the head and face. In particular, this protein plays a critical role in the development of a particular branch of cranial nerve III, which emerges from the brain and controls muscles that raise the eyes and eyelids. Mutations in the *KIF21A* gene likely alter the protein’s ability to transport materials within nerve cells, preventing the normal development of these cranial nerves and the extraocular muscles they control. Abnormal function of the extraocular muscles leads to restricted eye movement and related problems with vision.

Mutations in the *PHOX2A* gene cause CFEOM2. This gene provides instructions for making a protein that is found in the developing nervous system. Studies suggest that the PHOX2A protein plays a critical role in the development of cranial nerves III and IV,
which are necessary for normal eye movement. Mutations likely eliminate the function of the PHOX2A protein, which prevents the normal development of these cranial nerves and the extraocular muscles they control.

In most cases of CFEOM3, the genetic cause of the condition is unknown. Studies suggest that a gene associated with CFEOM3 may be located near one end of chromosome 16. The gene associated with Tukel syndrome has not been identified either, although researchers think that it may be located near one end of chromosome 21.

Inheritance Pattern

The different types of congenital fibrosis of the extraocular muscles have different patterns of inheritance. CFEOM1 and CFEOM3 are 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 result from new mutations in the gene and occur in people with no history of the disorder in their family.

CFEOM2 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. Tukel syndrome also appears to have an autosomal recessive pattern of inheritance, although the genetic change responsible for this disorder is unknown.

Other Names for This Condition

- CFEOM
- congenital external ophthalmoplegia
- congenital fibrosis of extraocular muscles
- congenital fibrosis syndrome
- general fibrosis syndrome

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting
Research Studies from ClinicalTrials.gov

• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22congenital+fibrosis+of+the+extraocular+muscles%22

Other Diagnosis and Management Resources

• GeneReview: Congenital Fibrosis of the Extraocular Muscles
  https://www.ncbi.nlm.nih.gov/books/NBK1348

• MedlinePlus Encyclopedia: Extraocular Muscle Function Testing
  https://medlineplus.gov/ency/article/003397.htm

• MedlinePlus Encyclopedia: Strabismus
  https://medlineplus.gov/ency/article/001004.htm

Additional Information & Resources

Health Information from MedlinePlus

• Encyclopedia: Extraocular Muscle Function Testing
  https://medlineplus.gov/ency/article/003397.htm

• Encyclopedia: Strabismus
  https://medlineplus.gov/ency/article/001004.htm

• Health Topic: Eye Movement Disorders
  https://medlineplus.gov/eyemovementdisorders.html

Genetic and Rare Diseases Information Center

• Congenital fibrosis of extraocular muscles

Additional NIH Resources

• National Eye Institute: Diagram of the Eye
  https://nei.nih.gov/health/eyediagram/

Educational Resources

• MalaCards: fibrosis of extraocular muscles, congenital, 1
  https://www.malacards.org/card/fibrosis_of_extraocular_muscles_congenital_1

• Merck Manual Consumer Version: Strabismus

• Neuromuscular Disease Center, Washington University
  https://neuromuscular.wustl.edu/syncm.html#feom
• Orphanet: Congenital fibrosis of extraocular muscles
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=45358

• The Engle Laboratory, Boston Children’s Hospital
  http://www.childrenshospital.org/Research/Labs/engle-laboratory/neurogenetics-
  research/cfeom-overview

Patient Support and Advocacy Resources

• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/congenital-fibrosis-of-the-extraocular-
  muscles/

• Prevent Blindness America
  https://www.preventblindness.org/

Clinical Information from GeneReviews

• Congenital Fibrosis of the Extraocular Muscles
  https://www.ncbi.nlm.nih.gov/books/NBK1348

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28congenital+fibrosis%5BTIAB
  %5D%29+AND+%28extraocular+muscles%5BTIAB%5D%29%29+OR+%28cfeom
  %5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+
  %22last+2520+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• FIBROSIS OF EXTRAOCULAR MUSCLES, CONGENITAL, 1
  http://omim.org/entry/135700

• FIBROSIS OF EXTRAOCULAR MUSCLES, CONGENITAL, 2
  http://omim.org/entry/602078

• FIBROSIS OF EXTRAOCULAR MUSCLES, CONGENITAL, 3A, WITH OR
  WITHOUT EXTRAOCULAR INVOLVEMENT
  http://omim.org/entry/600638

• TUKEL SYNDROME
  http://omim.org/entry/609428

Medical Genetics Database from MedGen

• Congenital fibrosis of the extraocular muscles
Sources for This Summary

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  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1736008/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16815872

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15671279

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10393037

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18214786

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10922204

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15621876


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