Oculopharyngeal muscular dystrophy

Oculopharyngeal muscular dystrophy is a genetic condition characterized by muscle weakness that begins in adulthood, typically after age 40. The term "oculopharyngeal" refers to the eyes (oculo-) and a part of the throat called the pharynx (-pharyngeal). Affected individuals usually first experience weakness of the muscles in both eyelids that causes droopy eyelids (ptosis). Ptosis can worsen over time, causing the eyelid to impair vision, and in some cases, limit eye movement. Along with ptosis, affected individuals develop weakness of the throat muscles that causes difficulty swallowing (dysphagia). Dysphagia begins with dry food, but over time, liquids can also become difficult to swallow. Dysphagia can cause saliva to accumulate and a wet-sounding voice. Many people with oculopharyngeal muscular dystrophy also have weakness and wasting (atrophy) of the tongue. These problems with food intake may cause malnutrition, choking, or a bacterial lung infection called aspiration pneumonia.

Individuals with oculopharyngeal muscular dystrophy frequently have weakness in the muscles near the center of the body (proximal muscles), particularly muscles in the shoulders, upper legs, and hips (limb-girdle muscles). The weakness slowly gets worse, and people may need the aid of a cane or a walker. Rarely, affected individuals need wheelchair assistance.

Rarely, individuals have a severe form of oculopharyngeal muscular dystrophy with muscle weakness that begins before age 45, and have trouble walking independently by age 60. These individuals often also have disturbances in nerve function (neuropathy), a gradual loss of intellectual functioning (cognitive decline), and psychiatric symptoms such as depression or strongly held false beliefs (delusions).

Frequency

In Europe, the prevalence of oculopharyngeal muscular dystrophy is estimated to be 1 in 100,000 people. This condition is much more common in the French-Canadian population of the Canadian province of Quebec, where it is estimated to affect 1 in 1,000 individuals. Oculopharyngeal muscular dystrophy is also seen more frequently in the Bukaran Jewish population of Israel, affecting 1 in 700 people.

Causes

Mutations in the *PABPN1* gene cause oculopharyngeal muscular dystrophy. The *PABPN1* gene provides instructions for making a protein that is found throughout the body. The PABPN1 protein plays an important role in processing molecules called messenger RNAs (mRNAs), which serve as genetic blueprints for making proteins. PABPN1 alters a region at the end of mRNA molecules that protects mRNA from being
broken down. The PABPN1 protein also is involved in transporting mRNA within the cell.

The PABPN1 protein contains an area where 10 copies of the protein building block (amino acid) alanine occur in a row. This stretch of alanines is known as a polyalanine tract. The role of the polyalanine tract in normal PABPN1 protein function is unknown. Mutations in the PABPN1 gene that cause oculopharyngeal muscular dystrophy result in a PABPN1 protein with an abnormally long (extended) polyalanine tract that includes between 11 and 18 alanines. Typically, affected individuals with shorter polyalanine tracts tend to have milder signs and symptoms that develop later in life compared to those with longer polyalanine tracts. The extra alanines cause the PABPN1 protein to form nonfunctional clumps within muscle cells. These clumps (called intranuclear inclusions) accumulate and are thought to impair the normal functioning of muscle cells, eventually causing cell death. The resulting loss of muscle cells over time most likely causes the muscle weakness seen in people with oculopharyngeal muscular dystrophy. In severe cases, it is likely that intranuclear inclusions affect nerve cells as well as muscle cells.

**Inheritance Pattern**

Most cases of oculopharyngeal muscular dystrophy are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. However, some individuals have mutations in both copies of the PABPN1 gene that lead to expanded polyalanine tracts. These individuals tend to have more severe signs and symptoms that develop earlier in life compared to individuals with a mutation in one copy of the gene.

In most cases, an affected person has one parent with the condition.

**Other Names for This Condition**

- dystrophy, oculopharyngeal muscular
- muscular dystrophy, oculopharyngeal
- oculopharyngeal dystrophy
- OPMD
- progressive muscular dystrophy, oculopharyngeal type

**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=%22oculopharyngeal+dystrophy%22

Other Diagnosis and Management Resources

- GeneReview: Oculopharyngeal Muscular Dystrophy
  https://www.ncbi.nlm.nih.gov/books/NBK1126
- MedlinePlus Encyclopedia: Ptosis
  https://medlineplus.gov/ency/article/001018.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Ptosis
  https://medlineplus.gov/ency/article/001018.htm
- Health Topic: Muscular Dystrophy
  https://medlineplus.gov/musculardystrophy.html
- Health Topic: Swallowing Disorders
  https://medlineplus.gov/swallowingdisorders.html

Genetic and Rare Diseases Information Center

- Oculopharyngeal muscular dystrophy

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Muscular Dystrophy
  https://www.ninds.nih.gov/Disorders/All-Disorders/Muscular-Dystrophy-Information-Page
- National Institute of Neurological Disorders and Stroke: Swallowing Disorders
  https://www.ninds.nih.gov/Disorders/All-Disorders/Swallowing-disorders-Information-Page
- National Institute on Deafness and Other Communication Disorders: Dysphagia
  https://www.nidcd.nih.gov/health/dysphagia

Educational Resources

- MalaCards: oculopharyngeal muscular dystrophy
  https://www.malacards.org/card/oculopharyngeal_muscular_dystrophy
- Orphanet: Oculopharyngeal muscular dystrophy
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=270
• The University of Arizona Health Sciences
http://disorders.eyes.arizona.edu/disorders/oculopharyngeal-muscular-dystrophy

• Washington University, St. Louis: Neuromuscular Disease Center
https://neuromuscular.wustl.edu/musdist/peeom.html#opd

Patient Support and Advocacy Resources
• Muscular Dystrophy Association
https://www.mda.org/disease/oculopharyngeal-muscular-dystrophy

• Muscular Dystrophy Canada

• Muscular Dystrophy UK
https://www.musculardystrophyuk.org/about-muscle-wasting-conditions/muscular-dystrophies/oculopharyngeal-muscular-dystrophy-opmd-factsheet/

• National Organization for Rare Disorders (NORD)
https://rarediseases.org/rare-diseases/oculopharyngeal-muscular-dystrophy/

Clinical Information from GeneReviews
• Oculopharyngeal Muscular Dystrophy
https://www.ncbi.nlm.nih.gov/books/NBK1126

Scientific Articles on PubMed
• PubMed
https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28oculopharyngeal+muscular+dystrophy%5BTIAB%5D%29+OR+%28OPMD%5BTI%5D%29%29+AND+english+%5BLa%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• OCULOPHARYNGEAL MUSCULAR DYSTROPHY
http://omim.org/entry/164300

Medical Genetics Database from MedGen
• Oculopharyngeal muscular dystrophy
Sources for This Summary


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U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services