Early-onset glaucoma

Description

Glaucoma is a group of eye disorders in which the optic nerves connecting the eyes and the brain are progressively damaged. This damage can lead to reduction in side (peripheral) vision and eventual blindness. Other signs and symptoms may include bulging eyes, excessive tearing, and abnormal sensitivity to light (photophobia). The term "early-onset glaucoma" may be used when the disorder appears before the age of 40.

In most people with glaucoma, the damage to the optic nerves is caused by increased pressure within the eyes (intraocular pressure). Intraocular pressure depends on a balance between fluid entering and leaving the eyes.

Usually glaucoma develops in older adults, in whom the risk of developing the disorder may be affected by a variety of medical conditions including high blood pressure (hypertension) and diabetes mellitus, as well as family history. The risk of early-onset glaucoma depends mainly on heredity.

Structural abnormalities that impede fluid drainage in the eye increase ocular pressure. These abnormalities may be present at birth and usually become apparent during the first year of life. Such structural abnormalities may be part of a genetic disorder that affects many body systems, called a syndrome. If glaucoma appears before the age of 3 without other associated abnormalities, it is called primary congenital glaucoma.

Other individuals experience early onset of primary open-angle glaucoma, the most common adult form of glaucoma. If primary open-angle glaucoma develops during childhood or early adulthood, it is called juvenile open-angle glaucoma.

Frequency

Primary congenital glaucoma affects approximately 1 in 10,000 people. Its frequency is higher in the Middle East. Juvenile open-angle glaucoma affects about 1 in 50,000 people. Primary open-angle glaucoma is much more common after the age of 40, affecting about 1 to 2 percent of the population worldwide.

Causes

Approximately 10 percent to 33 percent of people with juvenile open-angle glaucoma

have variants (also known as mutations) in the *MYOC* gene. *MYOC* gene variants have also been detected in some people with primary congenital glaucoma. The *MYOC* gene provides instructions for producing a protein called myocilin. Myocilin is found in certain structures of the eye, called the trabecular meshwork and the ciliary body, that regulate the intraocular pressure.

Researchers believe that myocilin functions together with other proteins in the eye as part of the extracellular matrix, which is an intricate lattice that forms in the space between cells and provides structural support. Variants may alter the protein in such a way that the protein is not part of the extracellular matrix. Defective myocilin that does not get incorporated in the extracellular matrix remains inside the cell. The defective protein may damage the cell, causing insufficient flow of fluid from the eye, resulting in increased intraocular pressure and causing the signs and symptoms of early-onset glaucoma.

Between 20 percent and 40 percent of people with primary congenital glaucoma have variants in the *CYP1B1* gene. *CYP1B1* gene variants have also been detected in some people with juvenile open-angle glaucoma. The *CYP1B1* gene provides instructions for producing a form of the cytochrome P450 protein. Like myocilin, this protein is found in the trabecular meshwork, ciliary body, and other structures of the eye.

It is not well understood how defects in the CYP1B1 protein cause signs and symptoms of glaucoma. Recent studies suggest that the defects may interfere with the early development of the trabecular meshwork, the tissue that regulates the secretion of fluid inside the eye.

Unknown variants in other genes may also be involved in early-onset glaucoma.

Learn more about the genes associated with Early-onset glaucoma

- CYP1B1
- MYOC

Inheritance

Early-onset glaucoma can have different inheritance patterns. Primary congenital glaucoma is usually inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have variants. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but do not show signs and symptoms of the condition.

Juvenile open-angle glaucoma 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 families, primary congenital glaucoma may also be inherited in an autosomal dominant pattern.

Other Names for This Condition

- Hereditary glaucoma

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Glaucoma of childhood (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2981140/)
- Genetic Testing Registry: Glaucoma 1, open angle, A (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1842028/)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- GLAUCOMA 1, OPEN ANGLE, A; GLC1A (https://omim.org/entry/137750)
- GLAUCOMA 3, PRIMARY CONGENITAL, A; GLC3A (https://omim.org/entry/231300)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(early-onset+glaucoma%5BTIAB%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D)

References

- Abu-Amero KK, Edward DP. Primary Congenital Glaucoma. 2004 Sep 30 [updated2017 Aug 17]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH,Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1135/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301314)
- Bayat B, Yazdani S, Alavi A, Chiani M, Chitsazian F, Tusi BK, Suri F,Narooie-Nejhad M, Sanati MH, Elahi E. Contributions of MYOC and CYP1B1 mutationsto JOAG. Mol Vis. 2008 Mar 13;14:508-17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18385784) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2268862/)
- Chavarria-Soley G, Sticht H, Aklillu E, Ingelman-Sundberg M, Pasutto F, ReisA, Rautenstrauss B. Mutations in CYP1B1 cause primary congenital glaucoma

byreduction of either activity or abundance of the enzyme. Hum Mutat. 2008Sep;29(9):1147-53. doi: 10.1002/humu.20786. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18470941)

- Chen Y, Jiang D, Yu L, Katz B, Zhang K, Wan B, Sun X. CYP1B1 and MYOCmutations in 116 Chinese patients with primary congenital glaucoma. ArchOphthalmol. 2008 Oct;126(10):1443-7. doi: 10.1001/archopht.126.10.1443. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18852424)
- Choudhary D, Jansson I, Sarfarazi M, Schenkman JB. Characterization of thebiochemical and structural phenotypes of four CYP1B1 mutations observed inindividuals with primary congenital glaucoma. Pharmacogenet Genomics. 2008Aug;18(8):665-76. doi: 10.1097/FPC.0b013e3282ff5a36. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18622259)
- Scelsi HF, Barlow BM, Saccuzzo EG, Lieberman RL. Common and rare myocilinvariants: Predicting glaucoma pathogenicity based on genetics, clinical, andlaboratory misfolding data. Hum Mutat. 2021 Aug;42(8):903-946. doi:10.1002/humu.24238. Epub 2021 Jun 24. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/34082484)
- Selvan H, Gupta S, Wiggs JL, Gupta V. Juvenile-onset open-angle glaucoma - Aclinical and genetic update. Surv Ophthalmol. 2022 Jul-Aug;67(4):1099-1117. doi: 10.1016/j.survophthal.2021.09.001. Epub 2021 Sep 16. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/34536459)
- Turalba AV, Chen TC. Clinical and genetic characteristics of primaryjuvenile-onset open-angle glaucoma (JOAG). Semin Ophthalmol. 2008Jan-Feb;23(1):19-25. doi: 10.1080/08820530701745199. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18214788)
- Vasiliou V, Gonzalez FJ. Role of CYP1B1 in glaucoma. Annu Rev PharmacolToxicol. 2008;48:333-58. doi: 10.1146/annurev.pharmtox.48.061807.154729. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17914928)

Last updated April 4, 2022