

Glaucoma, hereditary

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Creation Date: August 2002

Update: March 2004

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[Abstract](#)

[Keywords](#)

[Congenital glaucoma](#)

[Juvenile glaucoma](#)

[Adult-onset primary open-angle glaucoma](#)

[References](#)

Abstract

Hereditary forms of glaucoma include:

Congenital glaucoma appears in the first months of life, eventually at birth or in utero. Isolated congenital glaucoma is characterized by minor malformations of the irido-corneal angle of the anterior chamber of the eye. Clinical manifestations include tearing, photophobia and enlargement of the globe appearing in the first months of life. The etiology lies in an obstacle to aqueous humor outflow and the treatment is primarily surgical. Congenital glaucoma occurs in 1 of 10.000 births in Western Countries and the frequency is higher in some countries (especially in Middle East). Heredity is autosomal recessive, and the genes involved are CYP1B1, GLC3A and GLC3B.

Juvenile glaucoma, a primary open-angle glaucoma appearing during the first two decades of life, is characterized by elevated intraocular pressure, excavation of the optic nerve head, and amputation of the visual field. The treatment is medical and often surgical. The frequency is unknown but probably underestimated. Heredity is autosomal dominant, and the gene involved is MYOC.

Adult open-angle glaucoma is the most frequent form of glaucoma with clinical characteristics close to juvenile glaucoma, generally appearing after the age of 40 years. The etiology is probably multifactorial with a hereditary component. Several genes, including OPTN, are involved.

Keywords

Congenital glaucoma, trabeculodysgenesis, juvenile glaucoma, adult-onset primary open-angle glaucoma.

Hereditary forms of glaucoma include congenital, juvenile and, to a lesser extent, adult open-angle glaucoma.

Congenital glaucoma

Disease name and synonyms

The disease is sometimes termed trabeculodysgenesis or goniodysgenesis.

Excluded diseases

Excluded diseases are irido-trabeculodysgenesis, either peripheral as Axenfeld-Rieger syndrome, or central as [Peter's anomaly](#) or sclerocornea. Glaucoma related to

other ocular abnormalities can be excluded (aniridia, traumatic-, tumoral-, uveitic-, lens-induced glaucoma), as glaucoma related to a general disease ([Sturge-Weber](#), neurofibromatosis, [Rubinstein-Taybi](#), [Marfan](#)).

Definition

Congenital glaucoma corresponds to glaucoma appearing in the first months of life, eventually at birth or *in utero*. Isolated congenital glaucoma is characterized by minor malformations of the irido-corneal angle of the anterior chamber of the eye.

Diagnosis criteria / Clinical description

Congenital glaucoma diagnosis is first suspected by the occurrence of clear tearing, photophobia, enlargement of the globe (buphthalmos) and corneal edema, and then confirmed by examination under anesthesia. Examination under anesthesia allows measuring horizontal corneal diameter, intraocular pressure (IOP), echographic axial length and cup/disc ratio (optic nerve excavation) when the media are clear enough. The diagnosis is established by elevated IOP with corneal findings (enlargement of diameter, epithelial edema, horizontal breaks in Descemet's membrane), increased axial length according to age, and increased cup/disc ratio over 0.3. The disease is bilateral in 80% of cases.

Differential diagnosis

Differential diagnosis include:

- Megalocornea, with an isolated corneal diameter enlargement without IOP elevation and with a clear cornea.
- Sequelae of obstetrical trauma (forceps) with generally vertical breaks in Descemet's membrane.
- Congenital nasolacrimal duct obstruction, inducing tearing with frequent episodes of conjunctivitis (tearing is not always clear).
- Metabolic diseases leading to corneal opacities by accumulation of metabolites ([cystinosis](#), mucopolysaccharidosis).
- Primitive corneal dystrophies (congenital hereditary endothelial dystrophy).

Frequency

Congenital glaucoma occurs in 1 of 10.000 births in Western Countries and accounts for 2 to 15% cases among children in institutions for the blind. The frequency is higher in some countries (especially in Middle East).

Treatment

The treatment of congenital glaucoma is primarily surgical and appears as an emergency, since the corneal opacity can dramatically increase in a few days or hours. Interventions aim to facilitate the aqueous humor outflow in the irido-corneal angle towards the Schlemm's canal and the subconjunctival space. Goniotomy consists in introducing a needle in the anterior chamber to open the opposite side of the angle. Trabeculotomy creates a communication between Schlemm's canal and the anterior chamber. Trabeculectomy consists in the opening of the anterior chamber, under a scleral flap, to produce an aqueous humor outflow towards the subconjunctival space.

Nonpenetrating deep sclerectomy relies on the same principle, but without complete opening of the anterior chamber.

Topical medical treatment is an adjunctive therapy. Complementary treatments include repair of corneal opacities by transplantation and amblyopia therapy.

Etiology

The malformative etiology of primary congenital glaucoma has been previously considered to lie in the presence of a persistent membrane (described by Barkan in the 1950's) obstructing the iridocorneal angle. This gonioscopic appearance has been, however, difficult to prove by histological examination, and the obstacle to aqueous humor outflow seems in most cases to be located more externally in the trabeculum.

Genetics

Primary congenital glaucoma seems in most cases to be an autosomal recessive inherited disorder. Consanguinity is often present. Mutations in the *GLC3A* and *GLC3B* genes, located on chromosomes 2p21 and 1p36, respectively, have been described. *GLC3A* is related to the *CYP1B1* gene, which encodes the cytochrome P450 and is expressed in the trabecular meshwork, but its function remains unclear.

Juvenile glaucoma**Disease name and synonyms**

The disease is sometimes called presenile glaucoma.

Excluded diseases

Excluded diseases are closed-angle, pigmentary, pseudoexfoliation glaucoma. Glaucoma related to other ocular abnormalities or to a general disease (see section "Excluded diseases" in congenital glaucoma) can also be excluded.

Definition

Juvenile glaucoma is defined by a primary open-angle glaucoma appearing during the first two decades of life.

Diagnosis criteria / Clinical description

Juvenile glaucoma, like adult-onset primary open angle-glaucoma, is characterized by an elevated IOP with progressive excavation of the optic nerve head (cup/disc ratio) and amputation of the visual field. The disease is insidious at the beginning, especially considering that glaucoma is rare at that age, but can lead to blindness. IOP is often particularly high in juvenile glaucoma.

Differential diagnosis

Differential diagnosis can be made with optic atrophy (hereditary or secondary to metabolic, vascular or toxic mechanisms).

Frequency

The frequency of juvenile glaucoma is unknown but probably underestimated.

Treatment

The treatment is primarily medical (topical treatments reducing aqueous humor production or facilitating its outflow). The severity of IOP elevation often requires a surgical procedure (trabeculectomy).

Etiology

The exact mechanism underlying juvenile glaucoma remains unknown, but optic nerve head and trabecular meshwork seem to be the most involved structures.

Genetics

Juvenile glaucoma is inherited in an autosomal dominant pattern and is associated with mutations in the *MYOC* gene located in 1q23-25. This gene encodes the trabecular meshwork-induced glucocorticoid response protein (TIGR), which is expressed in the trabecular meshwork and ciliary body. TIGR is postulated to cause an IOP elevation by obstructing the outflow passages.

Adult-onset primary open-angle glaucoma**Disease name and synonyms**

Primary open-angle glaucoma.

Diagnosis criteria / Clinical description

Adult-onset primary open angle-glaucoma is the most frequent form of glaucoma, affecting 67 million people worldwide, and is the second cause of blindness. The disease generally appears after the age of 40 years and is characterized by clinical findings similar to those of juvenile glaucoma, *i.e.* elevated IOP with progressive excavation of the optic nerve head (Cup/disc ratio) and amputation of the visual field.

Treatment

The treatment is primarily medical (topical treatments reducing aqueous humor production or facilitating its outflow). Surgery is indicated (trabeculectomy) when disease progresses despite medical treatment.

Genetics

The hereditary nature of adult-onset primary open-angle glaucoma is not as clearly related to a mendelian inheritance as that of congenital or juvenile glaucoma. Nevertheless, first-degree relatives of an affected patient are 7 to 10 times more at risk than the general population. More than one gene is likely to be involved. Mutations in *OPTN*, a gene encoding the optineurin protein, have been recently identified. Optineurin is expressed in the trabecular meshwork, the non-pigmented ciliary epithelium and the retina. Its role could be neuroprotective.

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