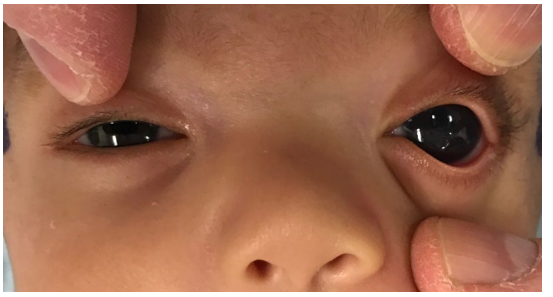
Characteristics and Management of Primary Congenital Glaucoma

Primary congenital glaucoma (PCG) is a rare but serious disease, accounting for up to 18% of childhood blindness.[1] Abnormal development of the anterior chamber angle leads to a decrease in trabecular meshwork outflow, resulting in elevated intraocular pressure (IOP).[2] The incidence of PCG varies from 1:10,000 in Western countries to 1:2,500 in Saudi Arabia and 1:1,250 among Slovakian Roma people.[1]

The majority of PCG occurs sporadically, but it can also be inherited in an autosomal recessive pattern.[2] Family history of PCG is reported in up to 40% of cases,[2] and several genes—primarily those encoding the enzyme cytochrome P450 1B1—have been associated with the disease.[1] PCG is classified by its age of onset, with neonatal-onset PCG manifesting between birth and 1 month of age, infantile-onset PCG occurring between 1 month and 2 years of age, and late-onset PCG manifesting after 2 years of age.[2]

PCG is typically bilateral, but it occurs asymmetrically in 30% of cases.[2] Its hallmark is elevated IOP. Other symptoms and signs may include epiphora, photophobia, blepharospasm, buphthalmos, corneal edema and enlargement, striae of the Descemet membrane, and optic nerve cupping.[2,3]

Medical management of PCG is not effective in the long term, and surgery is considered the definitive treatment. Goniotomy and trabeculotomy are standard first-line treatments for PCG due to their effectiveness in this patient population and their favorable safety profile. For refractory cases, more traditional glaucoma procedures may be required, including trabeculectomy or glaucoma drainage device (GDD) placement.[4] Left untreated, the disease will progress to blindness.[2]



***UNILATERAL DISEASE**. Infant with PCG in left eye.*

Diagnosis

Early diagnosis and treatment of PCG can improve a patient's visual outcome and mitigate PCG-associated symptoms. Accurate diagnosis requires a thorough history (including family history) as well as examination under anesthesia by an experienced clinician.

Clinical features. Most commonly, infants will present at less than 6 months of age with epiphora, photophobia, and blepharospasm.[4] These symptoms may also manifest as excessive eye rubbing and irritability.[4]

Elevated IOP in PCG is associated with corneal edema, possibly with corneal haze or central corneal scarring, and increased corneal diameter. The latter effect may lead to tears in the relatively inelastic Descemet membrane, known as Haab striae. These tears are most commonly horizontal or circumferential.

Because the young child's eye is more elastic than the adult's, increased IOP can also cause enlargement of the globe (buphthalmos). This may, in turn, lead to progressive myopia with or without astigmatism.

Finally, increased IOP can cause optic nerve cupping. Although this cupping can be reversed with successful control of IOP,[4] damage already done to the nerve fibers is not reversible.

Differential Diagnosis

Several congenital and acquired anterior segment conditions can mimic PCG.

Corneal dystrophies. If a patient has corneal haze and high IOP without buphthalmos, hereditary corneal opacities should be considered. Congenital hereditary endothelial dystrophy increases central corneal thickness, which can elevate measured IOP and cause corneal edema and corneal haze.

Other, rarer dystrophies to consider in patients with corneal haze without buphthalmos include severe posterior polymorphous corneal dystrophy (PPCD), congenital stromal corneal dystrophy, and posterior amorphous corneal dystrophy.

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Severe PPCD can also cause Descemet membrane tears, although they are typically vertical, unlike Haab striae in PCG. In addition, birth trauma from obstetric forceps may lead to membrane tears, which are usually vertical and unilateral.[4]

Megalocornea. Sometimes difficult to distinguish from buphthalmos, megalocornea is characterized by an enlarged cornea and anterior chamber without enlargement of the posterior chamber. Most commonly, it is a bilateral X-linked inherited disease. Typically, eyes with megalocornea will have large, clear corneas without breaks in the Descemet membrane.[4] Because these patients have normal posterior chambers, their axial lengths will be relatively normal.[4]

Congenital malformations. Anterior segment dysgeneses, a group of congenital disorders that cause malformations of the iris, cornea, or lens, may be mistaken for PCG. They may also cause a secondary glaucoma.[5]

One of these dysgeneses is Peters anomaly, a condition with varying degrees of central absence of corneal endothelium, Descemet membrane, and posterior corneal stroma. It may present with corneal opacity and cause secondary glaucoma. Similarly, sclerocornea, a nonprogressive corneal scleralization, may cause corneal opacity and secondary glaucoma, although the opacity is generally peripheral.

Medical Management

Medical therapy is not an effective long-term treatment for PCG and is generally used as a temporizing measure prior to surgery. Medications include beta-blockers (dosed once daily), carbonic anhydrase inhibitors, and prostaglandin analogues.[3]

Surgical Management

Procedures for PCG include angle surgery (goniotomy and trabeculotomy), trabeculectomy, GDD, and cyclophotocoagulation. The severity of the disease, as indicated by the size of the eye and amount of cupping, helps to dictate the treatment options.

Goniotomy and trabeculotomy. Both of these first-line treatments for PCG cut through the abnormal trabecular meshwork to increase outflow.[3] However, goniotomy requires a clear cornea, while trabeculotomy—in which a trabeculotome or illuminated microcatheter is inserted into and passed through Schlemm's canal—can be performed in patients with cloudy or opaque corneas.

The success rate for a single goniotomy has been reported to be 72%, and up to 94% with 2 goniotomies.[3] Trabeculotomy has been found to have similar success rates, although no randomized trial has yet compared these procedures.[2]

MIGS procedures. Goniotomy and trabeculotomy techniques have evolved over the years, and new microinvasive glaucoma surgery (MIGS) devices may enhance success rates while minimizing complications. Instruments such as the Trabectome (NeoMedix) or the Kahook Dual Blade (New World Medical) can serve as a replacement for a 23-gauge needle in goniotomy, and the TRAB 360 (Sight Science) may work as a more efficient trabeculotome.[5]

Gonioscopy-assisted transluminal trabeculotomy, in which an illuminated microcatheter is threaded through Schlemm's canal via an ab interno approach, is another way to perform a 360-degree trabeculotomy. It provides an appealing alternative because it spares the conjunctiva from scarring, thereby facilitating subsequent surgeries, if needed.[5]

GDD or trabeculectomy. When angle surgery fails, GDD placement or trabeculectomy with mitomycin-C (MMC) may be considered. Although these procedures show reasonable success rates in children, they carry significant risks and may be more difficult to perform in younger children.

Trabeculectomy success ranges from 50% to 87% in childhood glaucoma, depending largely on challenges with postoperative care.[3] A combined trabeculotomy-trabeculectomy procedure can be performed as well, and studies suggest it may be more successful than trabeculectomy alone.[3]

Success rates of GDD placement in children varies between 33% and 93% beyond 1 year of follow-up.[3] As with the aforementioned surgeries, the pediatric population presents unique challenges due to the reduced scleral rigidity and rather large size of these eyes.[5] GDD-related complications such as tube malposition, tube migration/retraction, and progressive capsular fibrosis occur more commonly in children than in adults.

New shunting devices. Implants developed for treating adult glaucoma, such as the XEN 45 Gel Stent (Allergan) and the investigational InnFocus MicroShunt (Santen), may be useful in PCG, but more study is needed.

Although these devices create blebs, they are more diffuse and posteriorly directed than GDD or trabeculectomy blebs, potentially reducing the risk of bleb leak or blebitis. Also, the small luminal diameter of these devices (XEN, 45 µm; InnFocus, 70 µm) may reduce the risk of hypotony. Both implants are made of a material that is well tolerated in the eye, but MMC is still needed to prevent scarring.

Conclusion

With variable symptoms and many similar congenital conditions, PCG presents a diagnostic and surgical challenge. When diagnosed early and treated appropriately, patients with PCG can enjoy a lifetime of vision. Though glaucoma surgeries have evolved over the last few decades, many are still challenging to perform in the pediatric population and carry significant risk. We continue to look for newer, safer management options.

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