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REVIEW PAPER

Primary congenital glaucoma

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ABSTRACT

Primary congenital glaucoma (PCG) is a developmental disorder affecting the trabecular meshwork and anterior chamber angle, leading to increased intraocular pressure (IOP) and potential vision loss. The early symptoms of PCG are already apparent during the first medical visits. Early diagnosis is crucial to be able to implement appropriate treatment to prevent the disease from developing as soon as possible. Its onset occurs before age three, with nonspecific symptoms such as eye rubbing, photophobia, and blepharospasm. Despite rare occurrence and heterogeneous prevalence depending on the geographical region, PCG accounts for a significant proportion of childhood blindness. The etiology of PCG involves genetic factors; the kinship of parents may increase its prevalence. Nonspecific symptoms of PCG necessitate vigilant examination to enable early detection. Diagnostic criteria include elevated IOP, optic nerve damage, corneal changes, and visual field defects. Treatment mainly relies on goniotomy and trabeculectomy in combination with pharmacotherapy.

KEY WORDS:

genetics, glaucoma, congenital, buphthalmos.

INTRODUCTION

Primary congenital glaucoma (PCG) is a childhood disorder that appears before the age of three. This age limit was estimated based on the growth of the eye, since by the age of three the eye is growing rapidly in response to changes in intraocular pressure (IOP) [1, 2]. Primary congenital glaucoma is caused by abnormal development of the trabecular meshwork (TM) and anterior chamber angle, resulting in obstruction of the physiological drainage of aqueous humor from the eye. This blockage can lead to increased IOP, resulting in abnormal development of eye tissues [1, 3].

The first documentation of PCG dates back to 400 BC, when Hippocrates observed unusual enlargement of the eyes of infants. In the early 18th century enlargement of the eyes of infants was linked to elevated intraocular pressure. Autopsies in the late 19th century and early 20th century showed distorted angle structures to be the cause of this condition. This discovery led to the development and introduction of goniotomy in 1938 by Barkan [1, 2].

Important clinical signs in PCG involve elevated IOP and noticeable changes in the optic nerve. However, other characteristic features, such as corneal enlargement and opacity, Haab's striae, and double vision, are also observed. It is important to note that not all symptoms are always present, and the elevated IOP can affect various parts of the eye. Children with PCG typically exhibit a set of three primary symptoms, referred to as the "clinical triad": epiphora, photophobia and blepharospasm. This can result in reduced visual acuity and loss of peripheral vision. Lack of treatment or late diagnosis leads to inevitable blindness [1, 2, 4].

The preferable treatment of PCG is surgery. Implementation of prompt treatment gives the child a chance of normal vision development. The choice of surgical technique depends on the type of abnormality of the drainage angle and the experience of the surgeon [5]. Mohamed F Farid's analysis of 49 cases of congenital glau-

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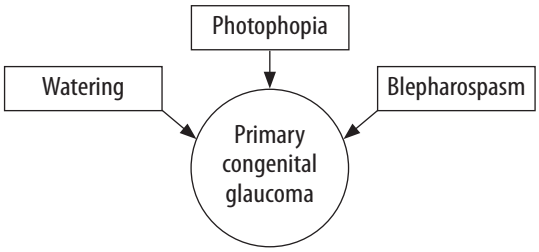

FIGURE 1. The classic triad of symptoms for primary congenital glaucoma

coma showed that operative success is better in early recognition of PCG, less advanced disease progression, and in children with lower mean IOP [6].

EPIDEMIOLOGY

The studies have shown that the majority of cases of PCG occur sporadically, although up to 40% are familial [7]. The prevalence of the disease varies geographically. In western countries the incidence of PCG is estimated between 1 : 10 000 and 1 : 20 000 live births. Incidence rates are higher in populations with higher levels of parental consanguinity. In Saudi Arabia the incidence of PCG is 1 in 2500 live births. Among Romani individuals, where there is a strong founder effect, the rate is 1 in 1250 live births [7–9].

Although PCG is a rare disease, it can lead to irreversible loss of sight. Among over 60 million affected people, 12 million are blind [10]. Primary congenital glaucoma accounts for 18% of childhood blindness [11].

ETIOLOGY

Primary congenital glaucoma is an inherited abnormality of the TM and anterior chamber angle. The majority of cases are sporadic, with no family history, but some cases of the disease can be inherited through an autosomal recessive pattern, with variable penetrance. The prevalence of the disease also appears to be higher in cultures where consanguinity is practiced [12]. Some chromosomal regions within which mutations occur are known. Five gene loci have been identified by linkage analyses: GLC3A, GLC3B, GLC3C, GLC3D, and GLC3E. Familial cases of glaucoma are most often associated with mutations in the CYP1B1 gene (encoding cytochrome P450 enzyme 1B1) located in the GLC3A region [13–15]. Although not all cases of PCG are genetically determined, children diagnosed with it should be referred to a genetic counseling center [16].

SYMPTOMS

Primary congenital glaucoma can be monocular or binocular, symmetrical or asymmetrical. This condition is typically detected either at birth or during the first months of life, with the majority of affected children presenting before 6 months of age. Classic symptoms are nonspecific and they include eye rubbing, irritability, discomfort and pain [1, 10, 17]. Attention should also be drawn to the triad of symptoms constituting photophobia, excessive tearing and tightening of the eyelids (blepharospasm). Parents or primary care physicians may occasionally observe abnormally enlarged eyeballs (buphthalmos), sudden whitening of the cornea and bluish discoloration of eyes in some cases. Other characteristic signs of PCG are elevated IOP, which can lead to optic nerve damage, increased corneal diameter and corneal opacity [12]. Moreover, there is a possibility of a decrease in visual acuity and/or restricted visual fields [1].

It is crucial to be vigilant for these clinical features in infants and young children to enable early detection and prompt management of the disease. The symptoms listed above, but especially eye asymmetry in newborns and infants, should raise the suspicion of PCG. In such cases, an ophthalmological examination should be carried out as soon as possible (Figure 1).

DIAGNOSIS

Congenital glaucoma can be uni- or bilateral, symmetrical or asymmetrical [18]. In PCG, there is a marked increase in the diameter of the cornea, which usually does not exceed 10 mm at birth. The transparency of the cornea is altered by stromal edema and followed by Haab's striae, which are horizontal ruptures of Descemet's membrane visible as threads. The axial length of the eye typically increases in cases of PCG and can be measured with ultrasound A [19]. At birth, the axial length does not exceed 18 mm and slowly grows to 22 mm at the age of 2. Increased axial length can be the cause of axial myopia, which can be one of the signs of PCG. The intraocular pressure among those patients is typically within the range of 30–40 mm Hg, but the lowering effect of anesthesia on IOP should be remembered. A history of congenital glaucoma among the child's siblings can be helpful in uncertain cases [19, 20].

The Childhood Glaucoma Research Network (CGRN) established an international classification to provide an organized and unified classification system of childhood glaucoma into seven subsets (glaucoma suspects plus 6 groups of childhood glaucoma, including PCG) [18].

The diagnosis is based on the presence of more than 2 of the following criteria:

- IOP of 21 mm Hg or more, preferably with a Perkins tonometer (a hand-held variant of Goldmann tonometer),
- glaucomatous optic nerve damage such as increased cupping, focal notching, or asymmetry of C/D (cup to disc ratio) more than 0.2 between the eyes,
- corneal changes (corneal diameter or Haab striae),
- visual field defects consistent with glaucomatous damage of the optic disc.

As noted previously, the CGRN classification allows suspicion of glaucoma but does not prove it in patients who meet at least one of the following criteria.

PCG is also classified according to the age of onset, as either neonatal (0–1 month), infantile (2–24 months), or late-onset or late-recognized (3–4 years) [21].

TREATMENT

Angle surgery, such as goniotomy or trabeculotomy, remains the preferred initial surgery for PCG. It is most successful in infantile-onset PCG, and less so in newborn or late-recognized PCG. The difference between goniotomy and trabeculotomy lies in the approach to the angle – goniotomy from an internal approach (*via* a paracentesis and instruments in the anterior chamber) and trabeculotomy from an external approach (using a scleral cut down to access the Schlemm canal) [22]. If angle surgery is not successful, trabeculectomy enhanced with mitomycin C or glaucoma implant surgery can be performed [22]. However, the type of surgical procedure depends on the disease severity, cornea clarity, severity of disease at the time of diagnosis and surgeon's choice [20].

Unlike in the case of adult glaucoma, medical therapy has a limited role and surgery remains the primary therapy [23]. In general, IOP-lowering medications work either by decreasing aqueous humor secretion or increasing it [1]. Medical therapy is typically used as an adjunct to surgery. It contains four groups of drugs: β-blockers – timolol and betaxolol; carbonic anhydrase inhibitors – dorzolamide; α2-agonists – brimonidine (contraindicated for children younger than 2 years of age and used with caution in children younger than six years of age, because these medications can cross the blood-brain barrier and may cause respiratory depression, apnea, and drowsiness); and prostaglandin analogs – latanoprost (not used in monotherapy) [20]. Timolol is the first choice in pediatric glaucoma. Also, the combination of timolol (once daily) and dorzolamide (twice daily) provides good control of the intraocular pressure [24].

It needs to be highlighted that regular life-long follow-up is necessary (every 6 months) for IOP monitoring and early detection of any surgery-related complications, because even if long-term IOP control from a surgical intervention is achieved, asymptomatic relapse can occur at any time [20]. For young patients, or patients with less than 2 years of IOP control, follow-up is recommended at least every 3–4 months.

CONCLUSIONS

Diagnosing and treating PCG early poses a challenge for both pediatricians and ophthalmologists. Primary congenital glaucoma is a rare but very significant disease, affecting children in the early years of life. This disorder is characterized by elevated IOP and potential eye tissue damage, with one notable feature being excessive enlargement of the eyeball. Early detection and management are vital to normalize IOP and prevent irreversible blindness. Diagnosis is based on clinical criteria such as elevated IOP, corneal changes, and glaucomatous optic nerve damage. The basis of treatment is surgical treatment, including interventions such as goniotomy or trabeculotomy. They can be followed by medical therapy if necessary. Regular life-long examination every 3–6 months is essential to monitor IOP and detect any complications. Genetic counseling should be considered due to the possible inherited nature of PCG. With increasing awareness, implementing early intervention, and ongoing research, we hope to reduce the negative effects of the disease, enhance the quality of life and improve vision of affected children. Further advances in genetics and surgical techniques offer promising prospects for managing this challenging condition.

It is essential to emphasize that pediatricians should promptly refer any newborn or infant with eye asymmetry for an ophthalmological evaluation.

DISCLOSURE

The authors declare no conflict of interest.

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