Pigmentary Glaucoma Treatment

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ABSTRACT

Pigment dispersion syndrome (PDS) is a clinical entity that is characterized with anomalous irido-zonular contact leading pigment dispersion throughout the anterior segment. Clinical presentation includes pigmented cells on the corneal endothelium, an increased pigmentation of the trabecular meshwork, and mid-periphery transillumination defects of iris. The syndrome is usually bilateral and more common in myopic individuals and young male adults. Also it can be associated with ocular hypertension or glaucoma. Pigmentary glaucoma (PG) is a kind of secondary open-angle glaucoma and is caused by occlusion of trabecular meshwork by pigmentary cells and reduction in the aqueous humor efflux. In this review, we will discuss clinical characteristics, pathogenesis and current management of PDS and PG.

Key words: Pigment dispersion syndrome, Pigmentary glaucoma.

INTRODUCTION

Pigmentary dispersion syndrome (PDS) and pigmentary glaucoma (PG) resulting from pigment scattering from posterior iris surface to anterior chamber due to damage of iris pigment epithelium comprises a disease spectrum which may lead elevated intraocular pressure (IOP) and vision loss. The PDS includes triad of pigmented cell accumulation on corneal endothelium (Krukenberg), cartwheel-like transillumination defects at mid-periphery of iris and dense, homogeneous pigment deposition in trabecular meshwork. If elevated IOP and glaucomatous disc damage are added to the triad, the disease is termed as PG.

The glaucoma developed in patients with pigment dispersion syndrome was first described as PG by H. Saul Sugar, denoting disease as a rare clinical entity.[1] It is known that PG accounts for 1-1.5% of all open-angle glaucoma in Caucasians.[1] Its incidence is lower in Far Eastern and Africans.

Pathogenesis

The reason underlying pigment accumulation in anterior segment and elevated IOP is pigment release resulting from friction of concave iris to zonules attached to anterior surface of lens.[4] It has been proposed that PDS-PG develops due to congenital migration anomalies in iris pigment epithelium or primary iris degeneration.[5] The widely accepted theory is degeneration of iris pigment epithelium as a result of genetic anomaly occurring at third trimester. This also explains more common peripheral retinal degeneration and retinal tears in patients with PDS-PG. Although autosomal inheritance pattern was detected in some families from Western Europe, several genetic inheritance patterns and responsible genes have been proposed.[6] Campbell indicated that reverse pupillary block caused by wide and thin iris in myopic eyes is involved in the physiopathology.[7] It was shown that iridolenticular contact acts as a check valve mechanism which allows humor aqueous flow from posterior segment to anterior segment but not vice versa and results in a pressure gradient pushing iris extremely posterior.[8] It was found that the iris concavity is increased during exercise and accommodation in patients with PDS-PG; that reversible pupil block becomes more prominent; and that the friction between iris and zonules is increased, causing more pigment discharge.

Pavlin et al. showed that iris concavity was further increased during to close fixation in PDS patients and that, after laser peripheral iridotomy, iris concavity disappeared and not changed by accommodation.[9] Similarly, Jensen et al.

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showed that iris concavity was increased after 10 minutes of cycling in PG patients and that, after laser peripheral iridotomy, iris concavity disappeared and not changed by exercise.[10]

In PG, it has been investigated which changes in iridocorneal angle cause IOP elevation. In this case, there is no occlusion of trabecular meshwork by free pigments. In a histological study, light and electron microscopy studies were performed in eyes donated by 3 patients with PG and trabecular specimens from 7 patients underwent trabeculectomy and it was shown that endothelial cell death develops due to phagocytosis of pigment by endothelial cells of trabecular meshwork (TM) and necrotic cells together with pigment were removed by macrophages. The loss of TM endothelium leads fusion of trabecular wall and collapse in trabecular space. The toxic-lytic enzymes released from death cells cause detachment of fibrils that ensure patency of Schlemm's canal (SC); thus, collapse of SC. Again, juxtacanalicular meshwork cells and endothelial SC cells are transformed into star cells, filling SC. Thus, IOP is elevated due to increased resistance against flow of humor aqueous via trabecular meshwork.

Conversion to pigmentary glaucoma from pigment dispersion

The conversion rate to pigmentary glaucoma has been reported as 35-50% among patients diagnosed as PDS in ophthalmology clinics.[2] In a population-based epidemiology study from Minnesota, conversion rate to PG was reported as 10% within 5 years and as 15% within 10 years in PDS patients.[3]

In PDS, risk factors for conversion to PG include:[2]

1. Family history: The PDS incidence was reported as 4.21% among patients with positive family history for PDS while PG incidence was reported as 26-48% among those with positive family history for glaucoma.

2. Gender: The male: female ratio is roughly equal in PDS; however, there is male preponderance in PG by 80-93%. In male patients, PG onset is 10 years earlier in average with more aggressive course.

3. Refractive error: Mean myopia level is higher in PDS patients with conversion to PG.

4. Krukenberg spindle: In PDS patients with marked Krukenbrg spindle, conversion to PG is more common.

5. Baseline IOP: It is most important risk factor and conversion rate is higher in PDS patients with baseline IOP≥21 mmHg (1.4 folds higher per 1 mmHg increase).[3]

6. Exercise: Excessive physical exercise lead an increase in iris concavity through elevated volume and pulse in the circulation of iris and choroid, which, in turn, increased pigment dispersion. However, there is limited study in this topic.

7. Accommodation: Iris concavity is increased during close fixation. This may increase pigment discharge. However, effect on conversion to PG is theoretical with variable effect on iris configuration.

Clinical features of pigmentary glaucoma

Pigment dispersion syndrome generally occurs at 20-40 years of age while PG occurs at 30-50 years of age. A type

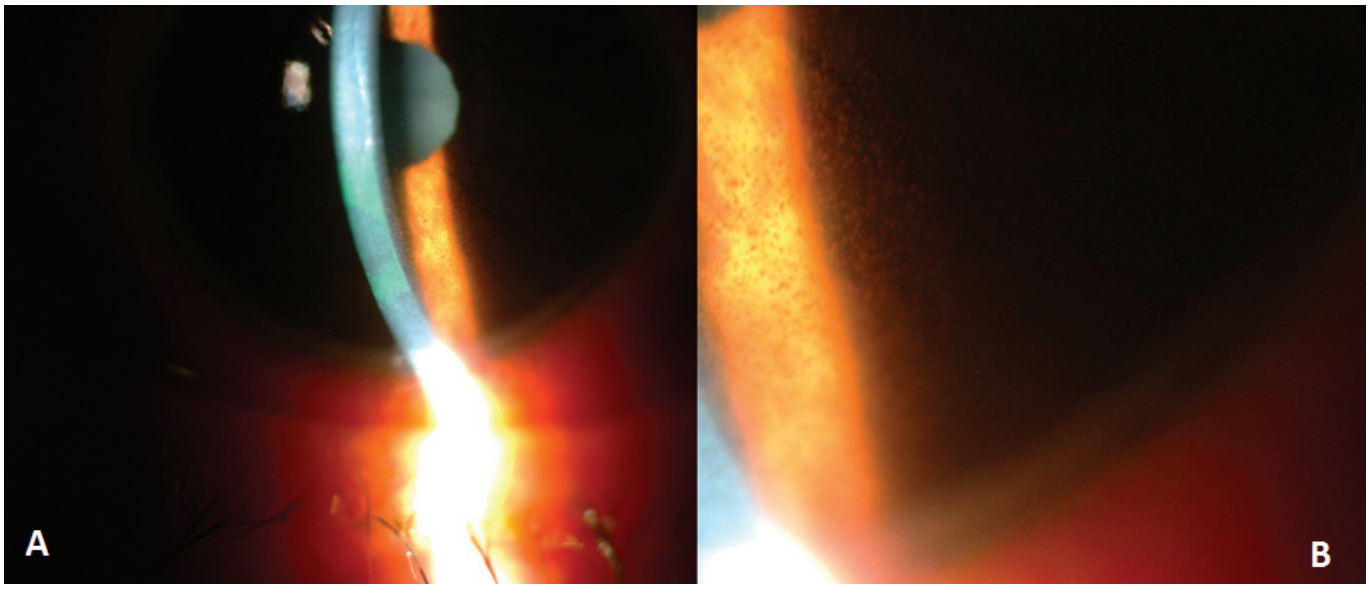

Figure 1. A- *Intense pigment cells at corneal epithelium in a case with pigment dispersion syndrome;* **B-** *magnified (by courtesy of Ufuk Elgin, MD).*

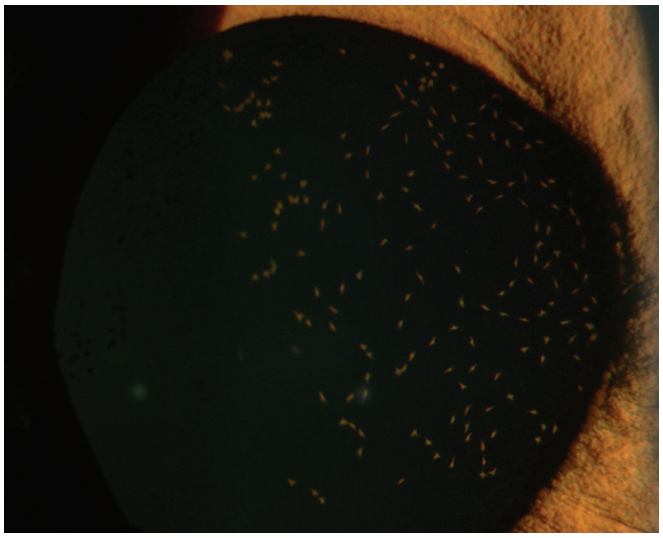

Figure 2. *Free pigment cells in anterior segment in a case with pigmentary glaucoma (by courtesy of Ufuk Elgin, MD).*

personality is more common in these cases. There is a male preponderance and 60% of patients with PDS and 80% of patients with PG are male. Myopia (3.9± 1.8 diopters) is seen in 80% of patients with PG.[3] At time of diagnosis, IOP is higher than primary open-angle glaucoma (POAG) (29±5 mmHg).

The patients present with headache caused by pigment release, IOP elevation and cornea edema following excessive physical exercise, impaired vision and halo.

Initially, the control of intraocular pressure is more challenging when compared to patients with primary open-angle glaucoma; thus, progression in visual field is more rapid. POAG-like changes occur in optic nerve and retinal nerve fiber layer (RNFL). Due to burnout phenomenon, PG can be more readily controlled after 10 years in average.[2] This is explained by decreased pigment discharge later on course of disease, facilitating IOP control.

Figure 3. *Image of atrophic iris with intense pigment release in a case with pigmentary glaucoma (by courtesy of Ufuk Elgin, MD).*

Treatment in pigment dispersion syndrome and pigmentary glaucoma

The therapeutic approach is similar to POAG. Treatment is tailored based on disease activity in individualized manner.

The patients with PDS or PG are classified into 4 groups according to disease activity:[12]

1. Inactive pigment dispersion and stable and/or low IOP

2. Active pigment dispersion and stable and/or low IOP

3. Active pigment dispersion with progressive glaucoma and elevated IOP

4. Inactive pigment dispersion with progressive glaucoma and normal and/or elevated IOP

The treatment should be more aggressive in patients within active phase while less intense therapies should be considered in patients within inactive phase or burnout period. The aim is to prevent conversion to PG in patients with PDS and to prevent progression in patients with PG.

First-line treatment is medical therapy as similar to POAG. In facts, parasympathomimetics are most effective and ideal agents in the topical treatment. Pilocarpine decreases reverse pupillary block by pupillary construction and prevents irido-zonular contact; thus, decreases pigment release substantially. In addition, it enhances aqueous efflux by stretching iridocorneal angle. However, it impairs vision due to accommodation spasms in PG patients who are largely young and it increases risk for retinal degeneration in patients who already have high-degree peripheral retinal degeneration. The complication such as cataract and systemic adverse events (dry mouth) cause them to be excluded from therapeutic choices.[13]

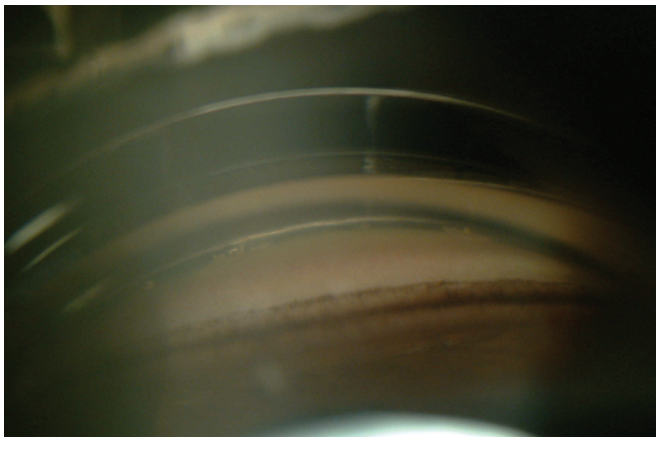

Figure 4. *Intense pigmentation at angle in a case with pigmentary glaucoma (by courtesy of Ufuk Elgin, MD).*

Beta-blockers can be used in the treatment of PG by decreasing production of humor aqueous effectively. However, topical prostaglandin analogs can also be preferred as first-line treatment as they enhance uveoscleral flow. Prostaglandins increase pigment production in melanocytes at iris stroma; however, they have no effect pigment epithelium at posterior surface of iris; thus, they do not increase pigment discharge.[15] Alpha agonists (brimonidine) and carbonic anhydrase inhibitors can be used effectively as adjuvant.

Laser therapies in pigment dispersion syndrome and pigmentary glaucoma

Argon laser trabeculoplasty (ALT) can be used in cases in which medical treatment is failed. However, intense pigmentation in TM causes excessive energy absorption, resulting in loss of initial effectiveness by rapid scarring. Better results can be achieved in younger patients.[16]

In a recent study, it was reported that, in PG patients, selective laser trabeculoplasty (SLT) achieved IOP reduction in 85% of patients by 20% at year 1 but the reduction persisted in only 14% of patients at year 2.[17] In addition, it was reported that there were cases underwent filtering surgery due to development of uncontrolled IOP elevation after SLT.[18] Thus, SLT should be carefully used in PG patients. Laser peripheral iridotomy (LPI) has been used in the PG treatment since 1984. However, it gains popularity after description of role of reverse pupillary block and iris concavity by Campbell and Karickhoof in 1990s.[7, 8] In US biomicroscopy studies, it was shown that LPI abolish reverse pupillary block by equalizing pressures of anterior and posterior chamber, correcting iris concavity. It is thought that this may prevent IOP elevation by reducing irido-zonular contact and pigment scattering. It is apparent that LPI will fail in patients with impaired trabecular anatomy due to excessive pigment deposition. There are studies with controversial results regarding prevention of progression of PDS to PG.

A recent meta-analysis addressed this issue.[19] In the meta-analysis it was concluded that there is no high-quality evidence that LPI prevents long-term vision loss in patients with PG and conversion to PG in PDS patients although it is a low-risk procedure. The reduction of iris concavity and irido-zonular contact can neither restore dysfunction already present in trabecular meshwork nor provide a significant improvement in visual function at long-term. However, it was reported that, at long-term, LPI can be have beneficial effects in eyes at risk for IOP elevation. Ideal eyes for LPI are those with marked iris concavity, visible pigment discharge following exercise or pupil dilatation or IOP elevation. In addition, contralateral eyes with PDS are also ideal candidate for LPI in patients with PG.[2] For example, in a case report from India, PDS was detected in a young male athlete presented with headache and halo following game; iris concavity was shown in UBM and normal IOP elevated up to 30 mmHg after game. In the patient, it was seen that iris concavity was restored and post-exercise excessive pigment discharge and IOP elevation were resolved after bilateral LPI.[20]

Surgery in pigmentary glaucoma

There is no sufficient study regarding minimal invasive glaucoma surgery (MIGS) in pigmentary glaucoma. In a study using second-generation iStent, it was reported that mean reduction of 35% in IOP was detected in POAG and pseudoexfoliation glaucoma groups and that uncontrolled IOP attacks and IOP elevation above 30 mmHg were developed in 3 patients with PG within first month, requiring trabectomy.[21]

In a prospective study, authors compared results of ab interno trabeculectomy via Trabectom between 101 eyes with POAG and 101 eyes with PG and found that IOP was 17.1 mmHg in PG group and 15.9 mmHg in POAG group at the end of year 1. The survival rate was 92% in PG group and 86% in POAG. A second surgery was required in 6 patients from PG group and 9 patients in POAG group. Authors concluded that Trabectom surgery is successful in PG patients and has comparable results with those in POAG.[22]

Trabeculectomy is gold standard in the surgical treatment of patients with PG.[23] In a prospective study on 18 PG eyes underwent trabeculectomy, it was reported that mean IOP was decreased from 34.5 to 13.7 mmHg and visual field and visual acuity were preserved for 8 years.[24]

CONCLUSION

PG has more rapid and progressive course when compared to POAG. Close monitorization is essential for both progression to PG from PDS and course of PG. LPI should be applied without delay in PDS accompanied by risk factors and marked pigment discharge with exercise and dilatation. STL should be attempted in cases with PG in which medical treatment is failed in IOP control. Surgical decision should be rapidly given in case of failure.

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