World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

44-year-old man with pigment dispersion syndrome related glaucoma: A case report & brief review

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World Journal of Advanced Research and Reviews, 2025, 25(03), 2335-2342

Publication history: Received on 16 January 2025; revised on 26 February 2025; accepted on 01 March 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.25.3.0612

Abstract

Background: Pigment dispersion syndrome (PDS) is quite common yet underdiagnosed. The condition itself is associated with the incidence of pigmentary glaucoma (PG) which poses a fatal consequence on the individual's sight. Thus, it is important to establish early detection and administer appropriate initial therapy to prevent further vision loss.

Case Presentation: A 44-year-old male was admitted due to worsening vision loss. History of wearing glasses, contact lenses, or eye trauma were denied. Patient was born with speech and hearing impairment along with pale colored left eye iris.

Summary: PDS has several complications including pigmentary glaucoma (PG) or pigment-related ocular hypertension (POHT). Imaging analysis with optical coherence tomography (OCT) examintation will be able to diagnose PDS from other diseases and might also aid as a monitoring device for associated glaucoma. The aim of treatment for PG itself is to stabilize IOP and controlling pigment dispersion.

Keywords: Pigment Dispersion Syndrome; Pigmentary Glaucoma; Intraocular Pressure; Optical Coherence Tomography

1. Introduction

Pigment dispersion syndrome, or in short PDS is usually produced by a spontaneous dispersion, release and deposition of iris' pigment into the anterior eye segment. Although this condition is relatively common, it usually is underdiagnosed as it may presents asymptomatic on some patients (1–3). However, a careful ophthalmologic examination is recommended to diagnose associated complications such as pigmentary glaucoma (PG) or pigment-related ocular hypertension (POHT) which might lead to vision loss.

2. Case report

A 44-year-old male was admitted to the ER with the chief complaint of gradual decrease of vision on the left eye since one month prior to admission, worsening faster during one week prior to admission. Previous similar complaint was denied. Symptom was accompanied by pulsing pain on the left eye. Nausea and vomiting were denied. There was no history of redness, hyper-lacrimation, discharge, nor foreign object sensation in the eye.

Patient had speech and hearing impairment since birth along with pale colored left eye iris. History of wearing glasses, contact lenses, or eye trauma were denied. History of diabetes and hypertension were also denied. Patient has never

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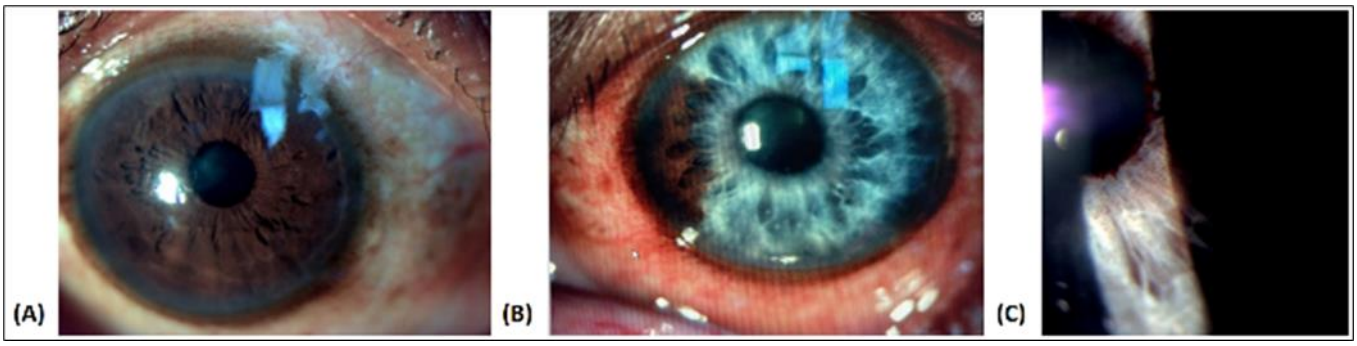
been medicated due to those conditions. History of similar illness within the family was denied. Patient was born via normal delivery under the care of midwife on the 9th month of gestation. Patient is currently working as a construction worker.



(A) Right eye showing clear cornea, dark iris, round pupil and clear lens (B) Left eye showing chemosis on the conjunctiva, iris is heterochromatic: light blue colored on the right side and dark brown colored on the left side (C) Krukenberg spindle visible: accumulation of pigments on the posterior iris of the anterior chamber

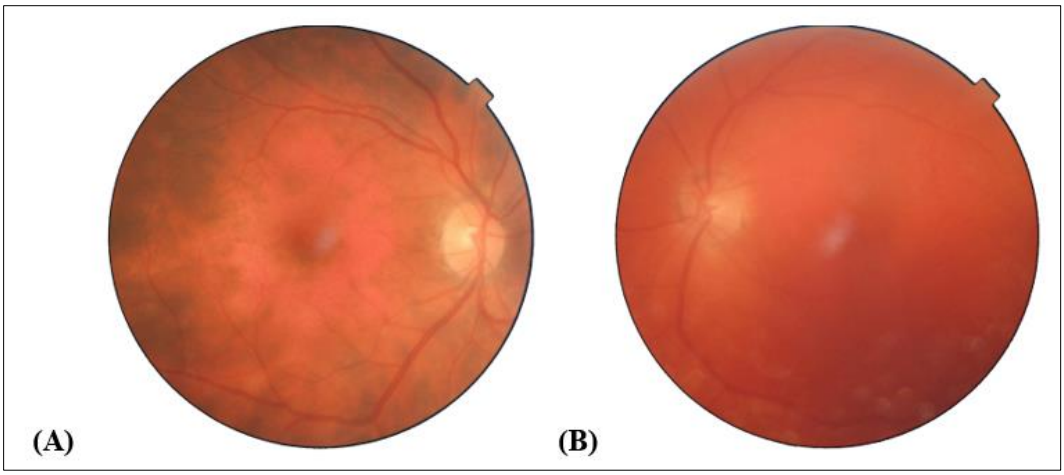
Figure 1 Slit lamp Anterior Segment Examination

Table 1 Anterior Segment Examination

OD	**Anterior Segment Examination**	**OS**
5/60	Vision	2/60
Edema (-)	Palpebra	Edema (-)
Hyperemia (-), chemosis (-)	Conjunctiva	Hyperemia (-), chemosis (+)
Clear	Cornea	Krukenberg spindle
Deep	COA	Deep
Round, chocolate in color	Iris	Not round, mostly chocolate in color, some lighter in color
Round, pupil reflect (+), RAPD (-)	Pupil	Not round, pupil reflect (+), RAPD (-)
Clear	Lens	Clear
Free in all directions	Eye Movement	Free in all directions
12 mmHg	TIO	35 mmHg

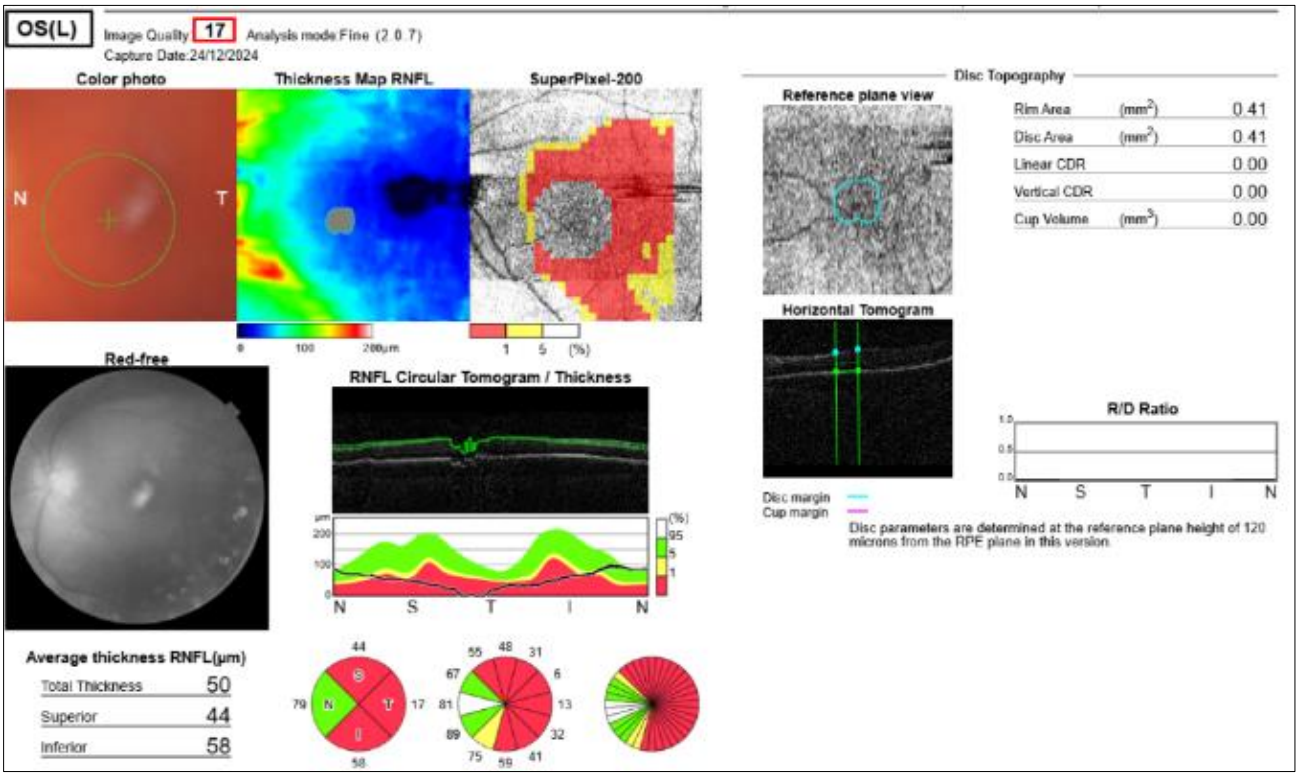
Throughout funduscopy examination, both eye's fundus reflex is positive, media is clear, and nervus 2 appears oranged colored, round shaped with clear border. Cup disc ratio is 0,3 without cupping. Artery: vein proportion is 2:3, without sclerosis and crossing present. There are also no exudate nor hemorrhage on the retina and macular foveal reflex are positive in both eye.

Patient is then diagnosed with left eye pigment dispersion syndrome and left eye open angle secondary glaucoma. He was prescribed 0,5% Timolol 2 x 1 drop, Acetazolamide 2 x 250 mg, and Potassium Chloride 1x600mg. After medicated, patient's TIO decrease from 35 to 11 on 2 weeks follow up, thus further therapy escalation is not needed.



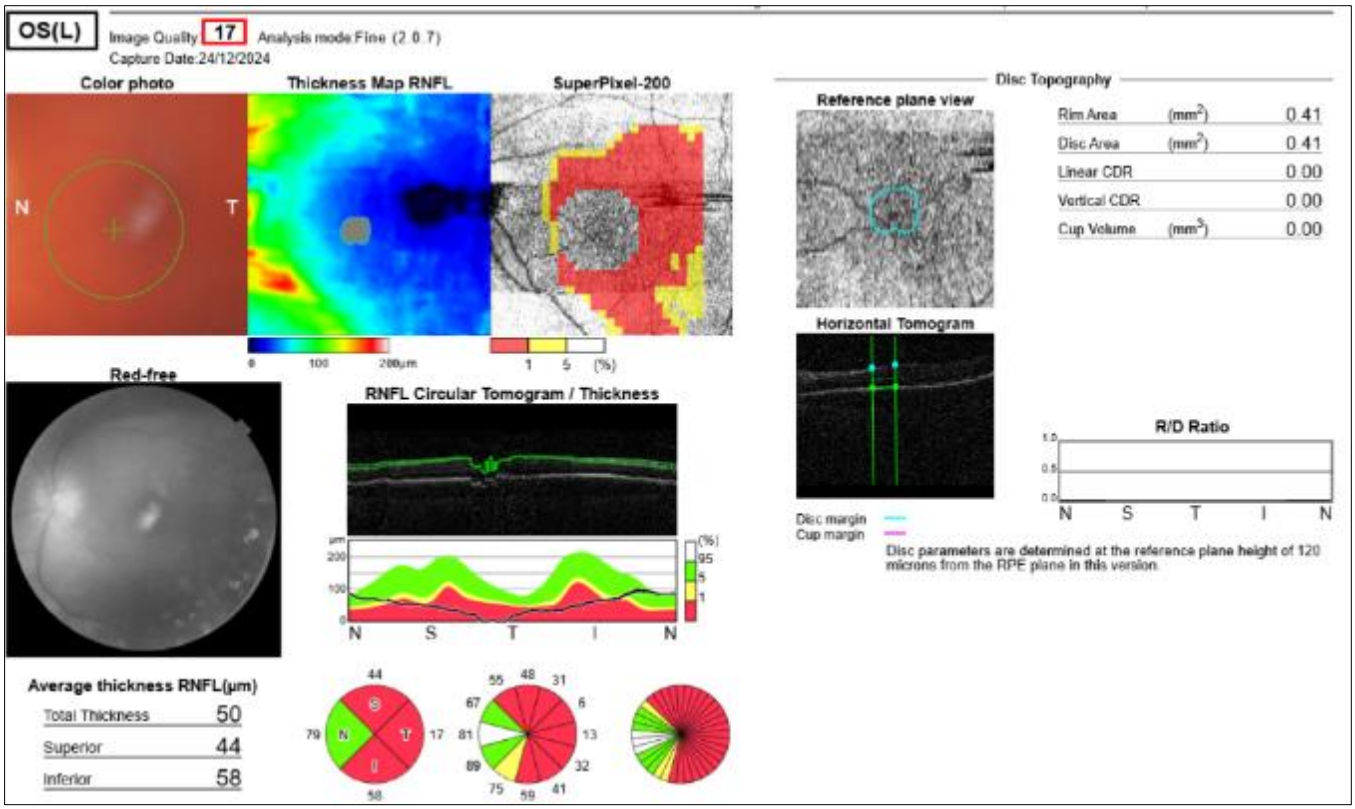
(A) Right eye (B) Left eye

Figure 2 Funduscopy Examination



Macula atrophy can be observed on the 3D disc report with topography

Figure 3 OCT report of the right eye



Macula atrophy can also be observed on the 3D disc report with topography

Figure 4 Right Eye OCT

3. Discussion

The hallmarks of PDS include the aberrant release of the posterior iris pigment epithelium and a noticeable buildup of that pigment in the anterior chamber (AC). PDS is characterised by a gonioscopically open angle, radial mid-peripheral iris transillumination defects that correspond with underlying zonular fibres, vertical pigment deposition on the corneal endothelium (Krukenberg spindle), and significantly increased pigmentation of the trabecular meshwork (TM) as seen by gonioscopy.

PDS itself is usually asymptomatic thus might presents as an accidental finding during routine examinations, especially on myopic patients. PDS is mostly bilateral, though asymmetry such as in this case might also be present in some cases. Symptoms varies ranging from milder ones especially on patients with normal IOP (red eye, slight discomfort) to a range of more severe symptoms (photophobia, blurred vision, halo vision, severe ocular pain). This condition is commonly found between the 3rd and 5th decade of life which match patient's age in this case (44 years old). Recent studies also shows racial disparity of associated complications (1,3).

Due to atrophy or degeneration of the iris pigment epithelium (IPE) or pigment loss from prenatal mesodermal dysgenesis, it was first believed that PDS and PG had a congenital aetiology. In other words, genetic plays as a huge factor. Studies have revealed a potential autosomal dominant inheritance for PDS and a multifactorial pattern of inheritance, which may contribute to the clinical manifestation of factors associated with iris colour, gender, and refractive error despite the low occurrence of familial PDS and PG. Numerous genetic loci have been linked to PDS by studies, including Based 7Q35-q36, OMIM ID 600510, Gene GPDS1 (glaucoma related PDS 1), and Glycoprotein nmb (GpnmbR150x) (1,3,4). However, there are also several other candidate genes reported such as PMEL which hightlights the role in melanosome function, melanin synthesis and storage which has an outstanding amount of evidence both from animal model studies and human genetics studies (5).

Besides PDS itself, patient in this case is also presented with complaints of deafness since birth. Although PDS itself is not related to hearing loss, there indeed are several syndromes which encompasses both PDS and hearing loss. However, none of those syndromes seems to fit the conditions of the patient reported within this case. The first syndrome which might cause both vision loss due to pigmentary glaucoma and hearing loss is Alport syndrome with

the triad of nephritis, deafness and ocular changes (6). However, patient doesn't experience the symptoms of macrohematuria or symptoms of chronic renal disease. Waardenburg syndrome is also characterized by sensory nerve deafness and deformities of pigmentation. But, pigment deformity in Waardenburg syndrome also happens on the skin (albinism), hair (white hair) and are usually present with other physical manifestations such as brow attachment and wide nasal root which are not present on this patient (7,8). Thus, those possibilities can be excluded.

Initial assessment for PDS may include slit lamp examination, IOP measurement, funduscopy, gonioscopy, and visual field analysis. Through slit lamp examination, it can be observed that pigment is not only deposited on the endothelium's surface; it is also phagocytosed by the endothelium and deposited in the KS (Krukenberg spindle), a vertical spindle-shaped island whose unique morphology is believed to be connected to the endothelium's phagocytosis of pigment and aqueous convection currents. It mostly is deposited on the inferior corneal endothelium. However, the entity is not pathognomonic and might not be present in all cases, as it's development are influenced by blinking and hormonal variations.

A spoke-like 360-degree iris transillumination defect (ITD) and a slightly concave midperipheral iris are also typical. ITD is one sign of pigment loss of the iris, it results from the iris pigment epithelium (IPE) in the middle of the iris rubbing against the lens zonule bundle complexes. When exposed to light, the iris in the pigment loss region manifests as radial mid-peripheral ITDs PDS patients usually have deep anterior chamber (AC) with free pigment frequently seen though not always present. The pigments must also be differentiated from inflammatory cells which are usually bigger, rounder, and whiter compared to the tanner brown and smaller particle with sharper corners. The anterior lens capsule may also experience pigment deposition. According to Scheie and Fleischhauer, pigment deposition may happen on the posterior capsule and lens zonules, also known as the "Scheie stripe." The Scheie line may occasionally appear as the initial indication of PDS. Long standing PDS however, might results in irregularity on pupil contour (1,2,9).

When evaluating PDS patients, gonioscopy and fundus examination are also crucial. The inferior trabecular meshwork frequently exhibits distinctive pigment deposition, and the angle is typically open. Compared to pseudoexfoliation syndrome, PDS exhibits more uniform trabecular meshwork pigmentation. Sometimes the Schwalbe line becomes pigmented, giving the appearance of a Sampaolesi line. PDS or pseudoexfoliation syndrome is characterised by the brown pigment known as the Sampaolesi line, which appears at or before the Schwalbe line. Although they are not always present, backward-bowing of the iris and an excess of iris processes are other significant gonioscopic findings in PDS (1,9).

However, recent study shows that clinical presentation and diagnosis of PDS might slightly vary between races. According to Pang et al., on white patient's PDS typical signs includes trabecular meshwork (TM) pigmentation, krukenberg spindle (KS), and iris transilumination defect (ITD). Major signs also include zonular/ lenticular pigmentation, anterior iris stromal pigment dusting, and posterior iris bowing. Diagnosis is made when there are at least two typical signs present. On black patients, typical signs include TM pigmentation and zonular/ lenticular pigmentation. KS is included in major sign. However, ITD, anterior iris stromal pigment dusting, and posterior iris bowing are minor signs. Diagnosis is made when TM pigmentation is present along with another typical/ major signs. While on asian patients, typical signs include TM pigmentation, zonular/lenticular pigmentation and KS (small triangle). Major sign includes posterior iris bowing. While ITD and anterior iris stromal pigment dusting are minor signs. Diagnosis is made when there are at least two typical signs presents (2).

Aside from clinical symptoms, some other patients may exhibit asymptomatic pigment dispersion episodes. Pigment release and clinical findings also vary greatly between patients; therefore, it is often underdiagnosed. Thus, additional examination such as ultrasound biomicroscopy (UBM) and optical coherence tomography (OCT) are needed. Detailed in vivo visualisation of the anterior segment structures is made possible by the UBM. The UBM assesses the connection between the peripheral iris and the zonular formations in the presence of light and accommodating pupillary reflexes, following physical activity, and scleral indentation. UBM findings includes concave iris configuration, increased iridolenticular contact area, increased distance from SS to iris insertion, increased lens thickness, and increased iris posterior bowing during accommodation. Anterior segment OCT (AS-OCT) findings usually includes increased AC volume, increased iridolenticular contact area, small iris volume-to-length ratio, increased AC depth, increased AOD, increased TISA (trabecular iris space area) at 500 μm and 750 μm from the scleral spur. For patients with elevated IOP, posterior segment OCT becomes a crucial tool to diagnose glaucoma with parameters such as changes in retinal nerve fiber layer and macular thinning. However, late in the progression of the disease, OCT measurements for the optic nerve are less helpful when the thickness of the nerve fibre layer reaches a floor effect of 40–50 mm without diminishing in any way. Nowadays, posterior-segment OCTA (OCT angiography) can be used to monitor glaucoma progression in correlation with visual field parameters (1).

As stated above, PDS however, may cause complications such as pigmentary glaucoma (PG) or pigment-related ocular hypertension (POHT). According to Pang et al., PG related to PDS are four times or more likely in Caucasians rather than Asians or Blacks (1,2). Other risk factors include family history of glaucoma in PG or PDS, male, presence of myopia, presence of KS in PDS, and initial IOP of more than 21 mmHg. PG symptoms are not easily distinguishable than other types of open-angle glaucoma. However, a key point which might distinguish PG is the probability where symptoms (i.e. vision loss) might occur either after or during exercise, especially in younger populations. Although PDS alone usually common yet presents with mild clinical symptoms, PG is rare yet have a severe effect on vision loss (1–3,10).

As stated above, OCT is crucial to analyze nerve fiber and ganglion complex, especially to identify glaucoma. Defects in the visual field and cupping of the optic nerve indicate PG. The anatomical damage in the retinal nerve fibre layer and ganglion cell complex seen in glaucomatous neuropathy must match the decline in the visual field. There are also visual field defects, which tend to worsen unless the IOP is adequately controlled. Visual field defects can be detected with greater sensitivity using the SITA-SWAP (blue on yellow) protocol. Controlling PG is more difficult than primary open-angle glaucoma. As with POHT guidelines, PG patients require rigid IOP monitoring and frequent follow-up. There is typically a phase of decreasing pigment liberation as PG changes over time. Over a ten-year period, Speakman reported normalising ocular pressure and decreased pigment dispersion. The term "pigment reversal sign" refers to this discovery. Darker trabecular meshwork is produced superiorly when inferior angle pigmentation tends to clear before superior angle. Patients with PG passing through this phase must be identified by regular gonioscopy and pressure monitoring. Therefore, determining when to stop anti-glaucoma treatment can be aided by the pigment reversal sign. Between 38 and 100 percent of people with PDS have myopia. Furthermore, the chance of acquiring PG increases with the degree of myopia (1).

Myopia is frequently also present in patient with PDS. Regardless of the degree of myopia, eyes with PDS are also more likely to experience retinal detachment. Males who are mildly myopic and phakic are most likely to experience retinal detachment. Though this incidence is not found on the patient presented on this case, indirect ophthalmoscopy using scleral depression and/or a three-mirror lens is crucial to look for any peripheral retinal abnormalities because lattice degeneration is also more common in PDS patients than in the general population (1,10).

Based on the IOP and pigment dispersion activity in PDS, there are four stages that has been described on previous studies: (1) stable IOP with inactive pigment dispersion; (2) stable IOP with active pigment dispersion; (3) PG and OHT with active pigment dispersion; and (4) PG and OHT or normal IOP with inactive pigment dispersion. Recent research has also suggested three clinical stages to help treat PDS: (1) asymptomatic pigment dispersion brought on by physiological factors like stress, exercise, and accommodation that do not cause OHT; (2) PG with noticeable pigment in TM and elevated IOP; (3) glaucomatous functional and morphologic damage; and pigment clearing from TM with normalising IP levels, which typically happens with ageing (3).

On the group with stable IOP without active pigment dispersion, observation is adequate. However, if active pigment dispersion is present, 2% Pilocarpine can be useful to control pigment dispersion as it changes the configuration of the iris. It is recommended to be administered eight-hourly. Reduction of physical activity, pharmacologic mydriasis and stress are also recommended as pigment dispersion are precipitated by exercise. If no high-risk factors for conversion to PG is present, routine monitoring of IOP and observation is adequate. However, if high-risk factors are present, the use of LPI (laser peripheral iridotomy) may be considered only on patients younger than 40 years with no POHT and iridozonular contact investigated by UBM. However, the method itself are still controversial and there still are insufficient evidence of its benefit. The majority of PDS patients have iris concavity and backward bending, which LPI lessens. Iris flattening by this procedure might reduce iridozonular contact and decreases the release of pigment into the anterior segment. By creating a pressure balance between the anterior and posterior chambers, this process limits the friction between the iris and zonular fibres. However, this method does not immediately address the low insertion and concavity of the iris, nor does it stop pigment exposure and damage to the trabecular meshwork (1).

The only treatment for groups with elevated IOP and/or optic neuropathy is going to be aimed at reducing IOP. In the pigmented races, reverse pupillary block and pigment dispersion call for more vigorous and violent treatment. Because of the large amount of pigment in the iris's IPE layer, pigment dispersion poses a serious risk to visual function in pigmented races like Asians, Africans, and people of colour (3).

The initial line of treatment for PG is hypotensive medication. The benefits of cholinergic agonists, like pilocarpine, include lowering IOP by promoting aqueous humour outflow, decreasing iridozonular contact, and decreasing pigment liberation by closing the pupil during miosis. Notwithstanding these potential benefits, pilocarpine use is restricted due to poor tolerance brought on by ocular surface disease, visual abnormalities linked to miosis, and the possible risk of retinal tears or detachment, especially in myopic individuals. Nowadays, safer medications frequently administered

includes beta-blockers, alpha agonists, and prostaglandin analogues. In a 12-month randomised clinical trial of individuals with PG, latanoprost outperformed timolol in lowering intraocular pressure. Prostaglandin analogues reduce intraocular pressure (IOP) by promoting uveoscleral flow, but they don't address the pigment liberation mechanism. PG treatment escalation is identical to POAG escalation. Alpha-adrenergic medications, b-adrenergic antagonists, and carbonic anhydrase inhibitors can all regulate intraocular pressure after prostaglandin analogues. If adequate IOP control is achieved, no further therapy escalation is needed, but close monitoring of IOP should be performed regularly (1). This initial treatment is in accordance with the medications prescribed in this case. Patient is treated with acetazolamide (a carbonic anhydrase inhibitor) and Timolol (a beta blocker). However, Acetazolamide may also induce hypokalemia and metabolic acidosis, both observed in humans and animals, thus Potassium Chloride is also administered in this patient (11,12). These medications are enough to lower patient's TIO from 35 to 11 on 2 weeks follow up, thus further therapy escalation is not needed

However, when IOP control is not achieved, escalation to laser therapy is typically sufficient when medicinal therapy is unable to do so. Selective laser trabeculoplasty (SLT) has gained popularity due to its safety profile, reproducibility, and capacity to drop intraocular pressure in a manner similar to that of medical therapy. According to a study on SLT treatment for PG, 85% of the eyes had a 20% decrease in IOP at one year, which dropped to 14% at two years. Thus, topical antiglaucoma medicine supplementation is usually required. The most frequent side effects in PG eyes treated with SLT are inflammation and IOP spikes. High-risk variables for post-SLT IOP increase involves having a history of argon laser trabeculoplasty, using several topical medicines, and having highly pigmented TM. And ophthalmologist must choose the least amount of energy to create bubbles (usually 0,4 mJ/spot). To identify IOP increases (>6 mmHg), IOP should be measured 1-hour post treatment to decide whether alpha-agonist hypotensive treatment is needed. Short-term topical antiinflamatory 0,5% Ketorolac QID for 5 days or 1% Prednisone acetate QID for 5 days are advised as they were reported to increase the effectiveness of SLT (1).

If inadequate IOP control with progressing visual defect are still present, surgical therapy should be considered. The first line of treatment for advanced or uncontrolled PG is still filtering surgery. Antifibrotic medications are used intraoperatively to minimize anterior chamber swelling, reduce vitreous base and peripheral retinal tension, and prevent bleb scarring. Aqueous shunts are not used as a primary operation; rather, they are reserved for eyes when trabeculectomy has failed. By shunting aqueous past the clogged trabecular meshwork into the Schlemm canal, minimally invasive glaucoma surgery (MIGS) procedures provide a higher safety profile than standard glaucoma surgery and prevent the production of blebs. Some examples of MIGS includes Trabectome ®, Kahook ®, and iStent ® (1).

4. Conclusion

PDS has several complications including pigmentary glaucoma (PG) or pigment-related ocular hypertension (POHT). Imaging analysis with ultrasound biomicroscopy (UBM) and optical coherence tomography (OCT) examintation will be able to diagnose PDS from other diseases and might also aid as a monitoring device for associated glaucoma. The aim of treatment for PG itself is to stabilize IOP and controlling pigment dispersion.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from individual included in this study.

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