GNZ 2024 CME Cases and MCQs

Case: Pigmentary glaucoma

Learning outcomes

- Demonstrate an understanding of the differences between pigment dispersion syndrome, pigmentary ocular hypertension, and pigmentary glaucoma
- Analyse, interpret and correlate the findings with the diagnosis of pigmentary glaucoma
- Discuss treatment options and different treatment modalities for pigmentary glaucoma

Case history

A 68 year-old Caucasian male presents to your practice for a glaucoma assessment. He mentions having used eye drops in the past. He cannot remember their name but stopped 1-2 years ago. He also mentions undergoing some kind of laser treatment to the eyes but cannot remember why. He still wears glasses but usually removes them for reading. He has good general health and is not taking any medications. His family history includes glaucoma in his mother, diagnosed around age 70 and currently uses eye drops.

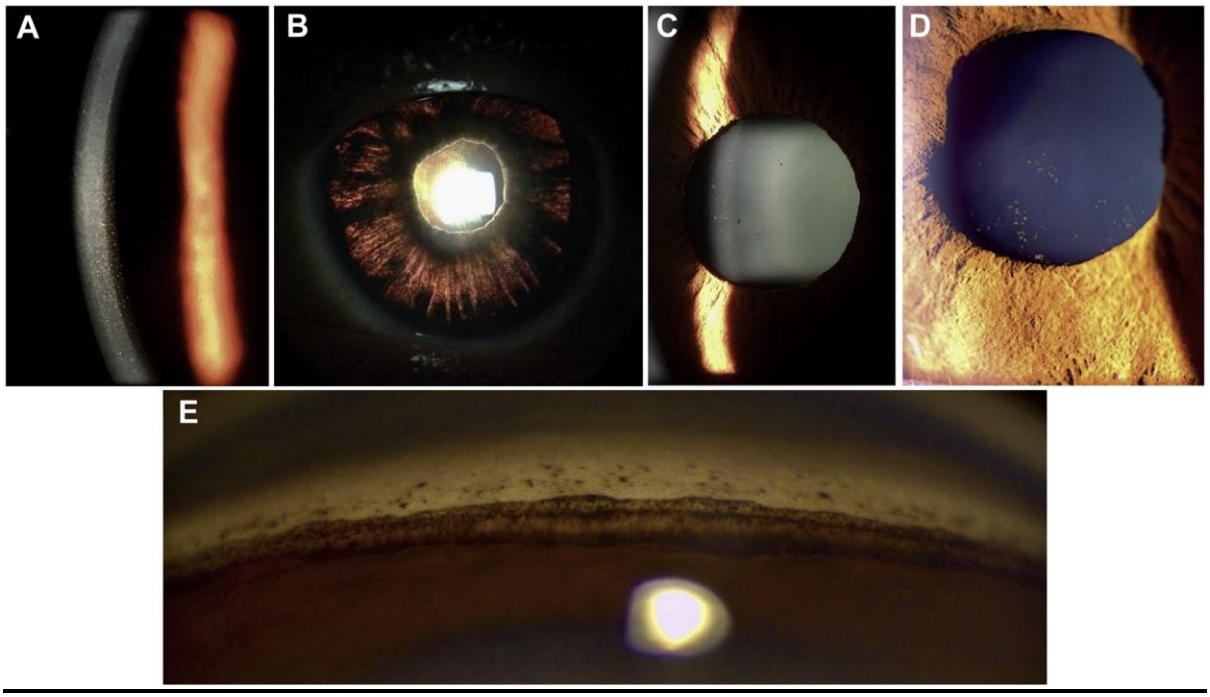
Your examination findings on presentation shown below.

Table 1: Clinical examination findings

	Right eye	**Left eye**
Best corrected visual acuity	6/6	6/7.5
Subjective refraction	-3.00/-1.50 x 156	-3.75/-0.50 x 012
Intraocular pressure Goldmanns	28 mmHg	30 mmHg
Perkins Pachymetry	537 µm	541 µm
Ishihara	14/14 plates	14/14 plates
Pupils	Small L RAPD	
Slit lamp examination (See Figures 1 and 2)	Corneal endothelial pigment and spoke-like mid-peripheral iris transillumination defects on retroillumination Patent peripheral iridotomy at 12 o'clock	Corneal endothelial pigment and spoke-like mid-peripheral iris transillumination defects on retroillumination Patent peripheral iridotomy at 12 o'clock

Figure 1: Composite image of anterior segment

Composite image of the anterior segment clinical findings. (Reproduced from Bustamante-Arias et al 2021)



Question 1

Describe the clinical photographs seen in Figure 1.

Answer:

Composite photographs in Figure 1 show:

A) Brown, wedge-shaped pigment deposition along the inferior endothelial surface, also known as Krukenberg spindle
B) Spokelike 360 degree iris transillumination defects seen by retro illumination technique
C) Pigment deposition on the anterior capsule of the lens
D) Loss of continuity and irregular pupil contour associated with pigment on the anterior capsule of the lens
E) Indirect gonioscopy image of an open angle showing heavy homogeneous pigmentation of the trabecular meshwork

End of answer

Question 2

Based on the initial history and examination, what is your working diagnosis?

Answer:
The most likely initial diagnosis is pigment dispersion syndrome (PDS), pigmentary ocular hypertension, or pigmentary glaucoma. While PDS typically affects younger (20-45 year old) Caucasian males, the patient may have had the condition for some time before presenting.

Characteristic features of PDS include::

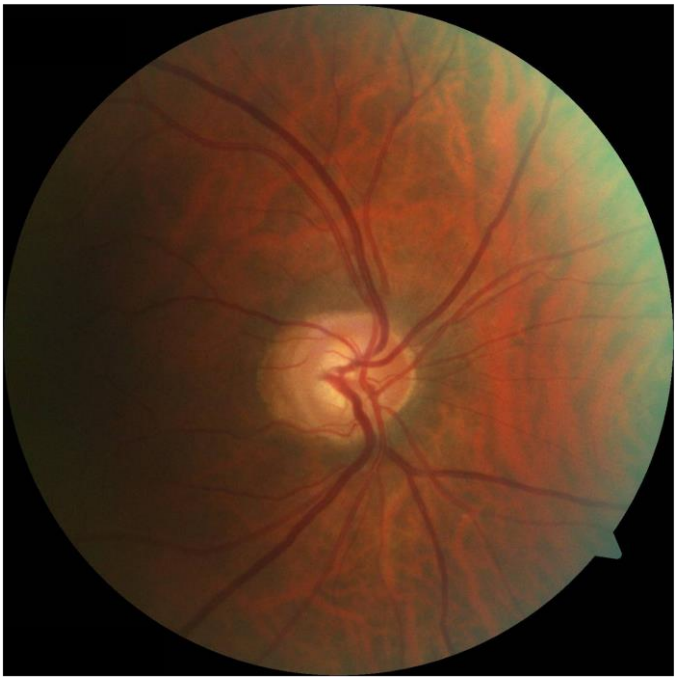
- Kruckenberg's spindle
- Spoke-like mid-peripheral iris transillumination defects
- Posterior bowing of the iris, heavily pigmented trabecular meshwork, and a darkly pigmented line anterior to the trabecular meshwork (Sampaolesi's line)

Although the patient's history of using eye drops suggests a possible prior diagnosis of pigmentary glaucoma, further testing is necessary for confirmation. It is crucial to assess the structure and function of the optic nerve. Clinical optic disc assessment, visual fields and OCT of the peripapillary retinal nerve fibre layer and macular were also performed.

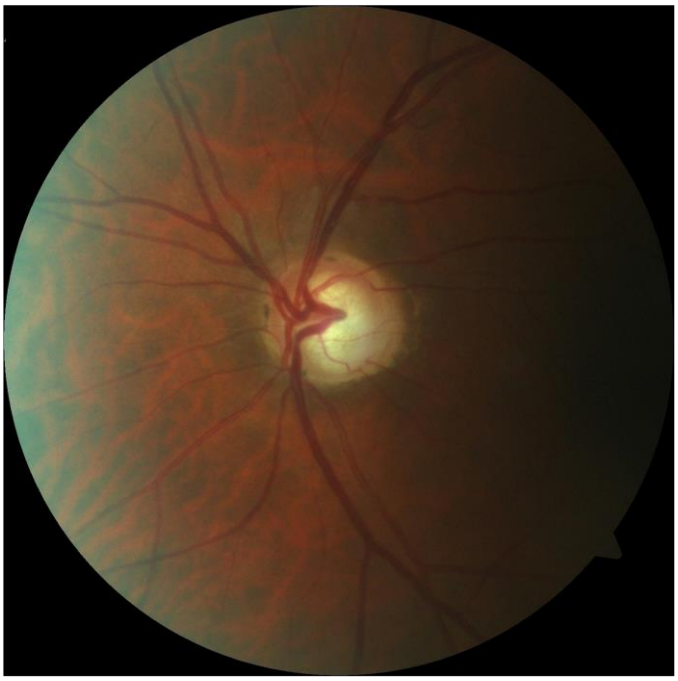
End of answer

Figure 2: Colour photos of right and left optic nerve heads

Right eye



Left eye



Question 3

Describe the above optic nerve head photos.

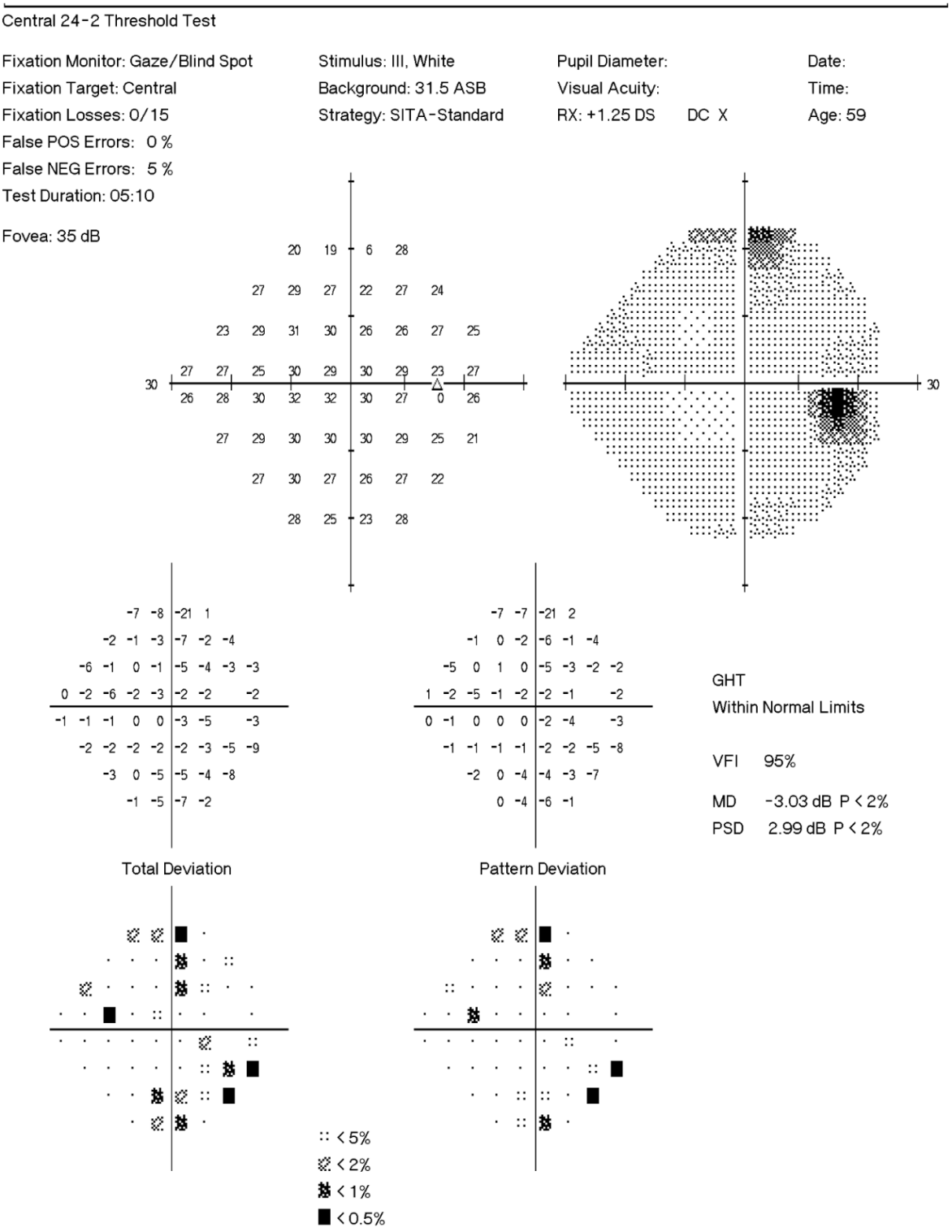
Answer:
The optic disc photographs show some asymmetry. Both nerves are of an average size. The right optic nerve shows a generalised enlargement of the optic cup, with a cup-to-disc ratio of approximately 0.8, with temporal peripapillary atrophy. There is no focal loss (notching) of rim tissue, although the neuroretinal rim is thin both superiorly and inferiorly. There is no disc haemorrhage.

The left optic nerve shows focal thinning of the rim inferiorly, with an inferior notch. There is also thinning of the neuroretinal rim superiorly, although there is no notch in this region. The cup-to-disc ratio is approximately 0.9, and there is temporal peripapillary atrophy. There is no optic disc haemorrhage.

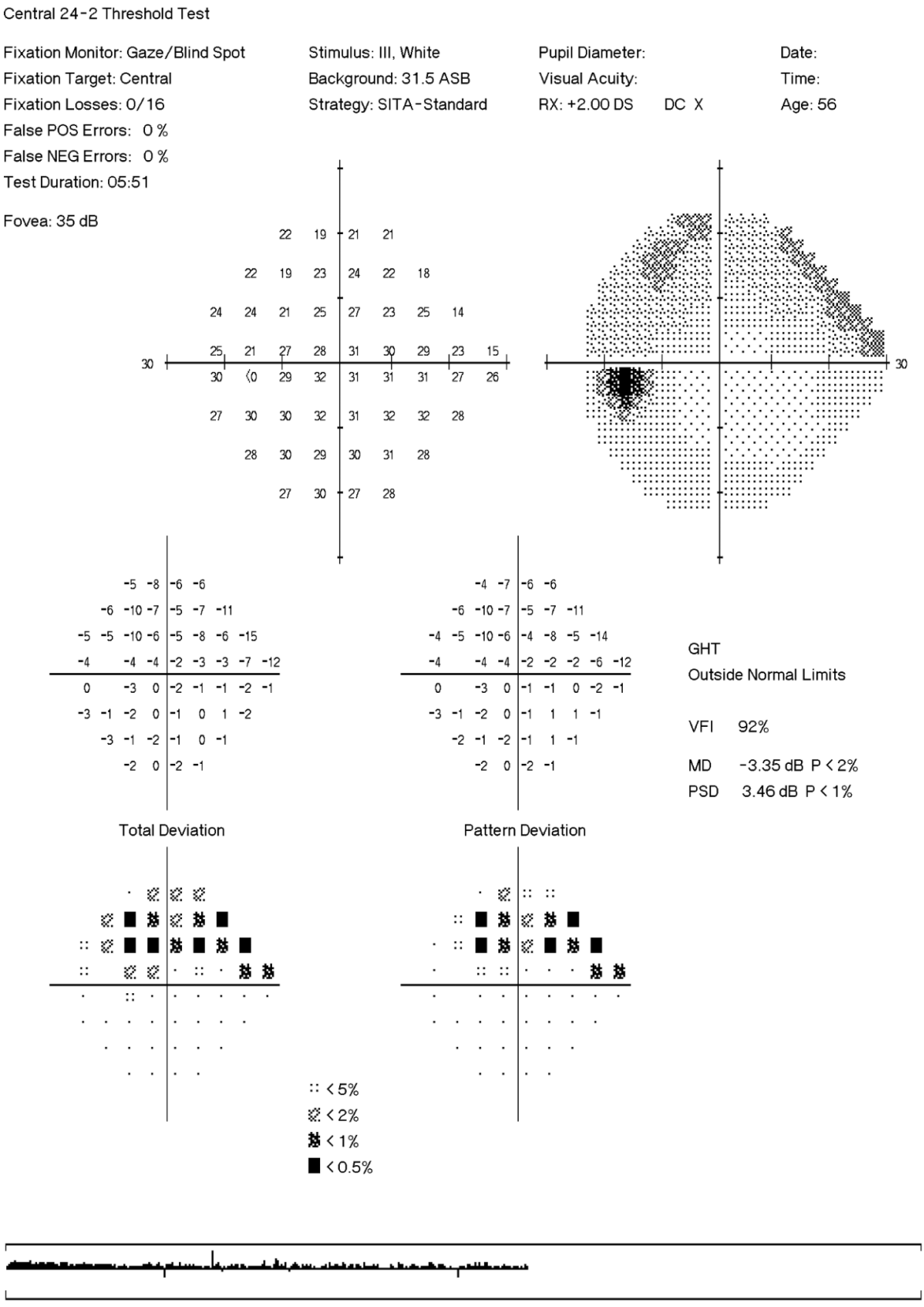
End of answer

Figure 3: Visual field images

Right eye



Left eye


Central 24-2 Threshold Test
Fixation Monitor: Gaze/Blind Spot
Fixation Target: Central
Fixation Losses: 0/16
False POS Errors: 0 %
False NEG Errors: 0 %
Test Duration: 05:51
Fovea: 35 dB
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard
Pupil Diameter:
Visual Acuity:
RX: +2.00 DS
DC X
Date:
Time:
Age: 56
GHT
Outside Normal Limits
VFI 92%
MD -3.35 dB P < 2%
PSD 3.46 dB P < 1%
Total Deviation
Pattern Deviation
:: < 5%
< 2%
< 1%
< 0.5%

Question 4

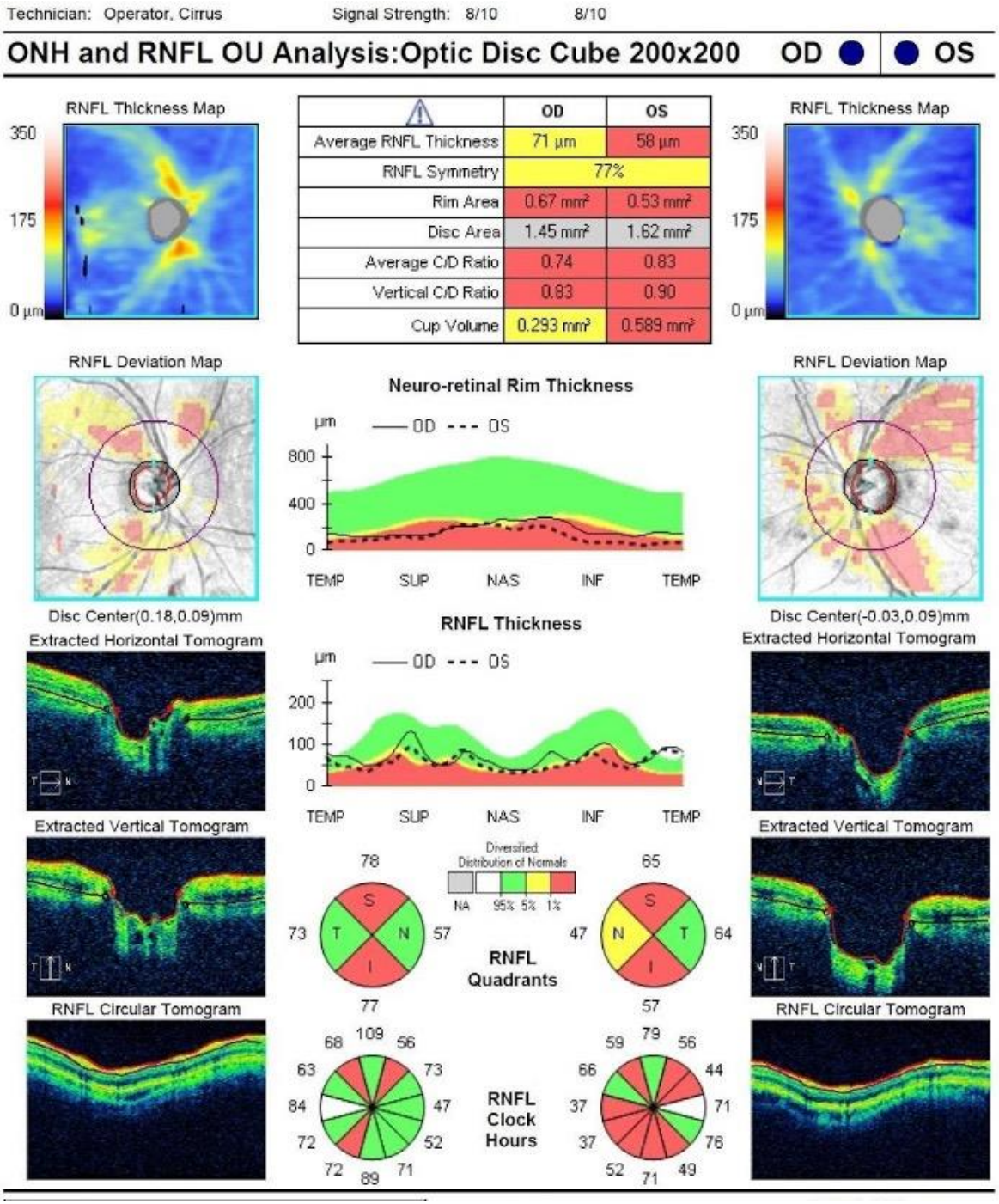
Describe this patient's visual field tests.

Answer:
A SITA-standard 24-2 visual field was performed in both eyes, with good reliability indices. In the right eye visual field, there are a few scattered points with reduced sensitivity values compared to an age-matched normative database. However there is no glaucomatous pattern to the visual field. The glaucoma hemifield test is within normal limits.

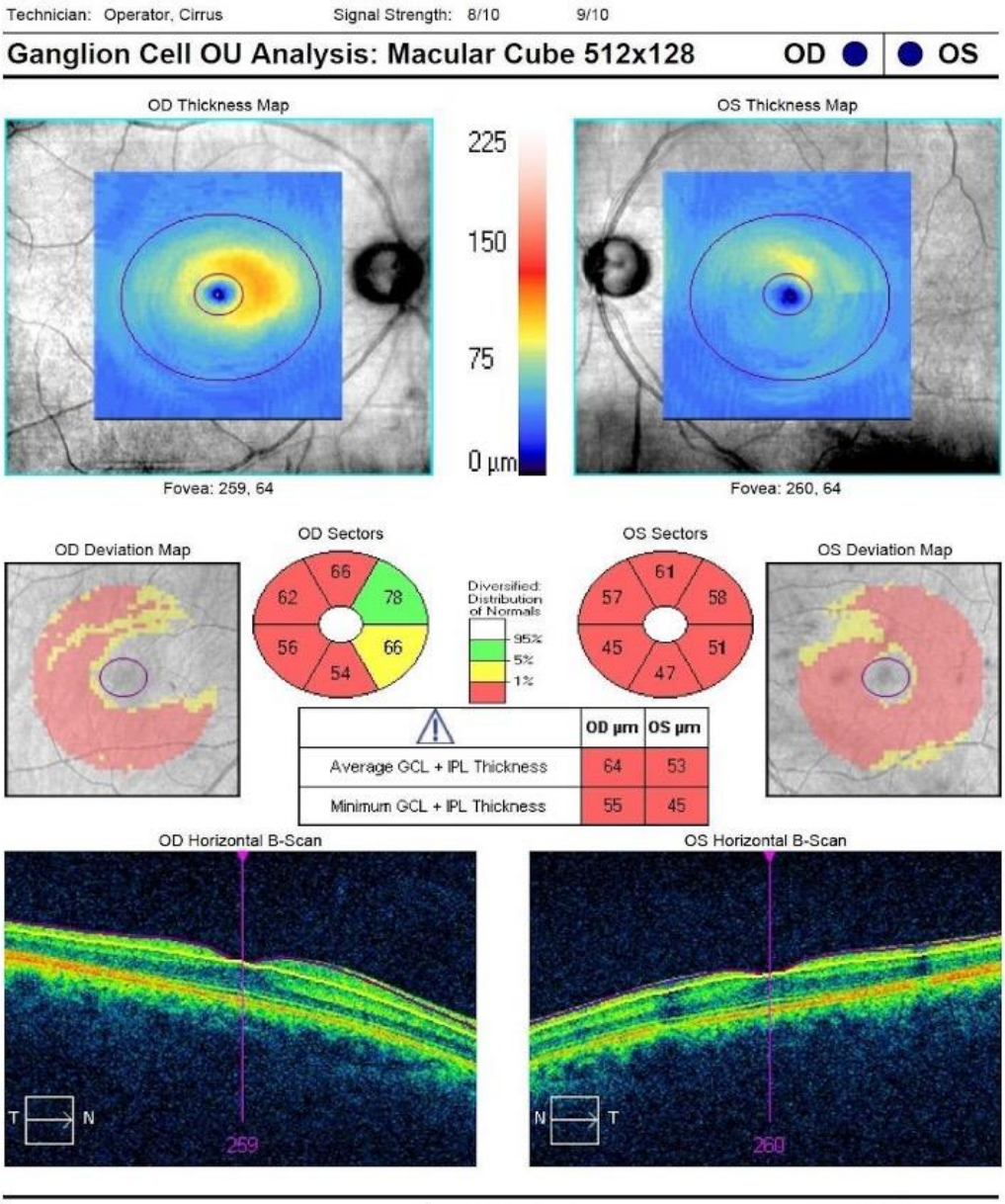
The left eye shows a superior arcuate-type defect, affecting the superior-nasal quadrant more than the superior-temporal quadrant. There is no immediate threat to fixation. The glaucoma hemifield test is outside normal limits.

End of answer

Figure 4: Retinal nerve fibre layer OCT scan analysis both eyes



OCT macular scan ganglion cell complex both eyes



Question 5

Describe this patient's RNFL OCT scans and Ganglion cell layer scan

Answer

The RNFL OCT scans are of adequate quality with no segmentation errors or movement artefacts. The optic disc OCT scan further emphasises the asymmetry

between the two eyes. Both eyes show a generalised loss of superior and inferior retinal nerve fibres in both eyes, with more pronounced loss in the left eye, corresponding to the observed thinning of the neuroretinal rim. Additionally, the scan shows that the optic cup is more excavated in the left eye.

The ganglion cell complex (GCC) scan, also of good quality, reveals diffuse thinning of the GCC (including the ganglion cell layer and inner plexiform layer) in both eyes. However, the thinning is more pronounced in the left eye, consistent with the findings on the RNFL OCT and visual field. Furthermore, there is no macular pathology that could confound scan results.

Based on the clinical examination, history, visual field results, and OCT scans, the patient has pigmentary glaucoma, affecting the left eye more than the right eye. The clinical examination and history are consistent with the identified visual field loss and OCT abnormalities. No other causes for visual field loss and OCT findings could be identified.

Question 6

What is the difference between pigment dispersion syndrome, pigmentary ocular hypertension (POHT), and pigmentary glaucoma?

Answer:
Pigment dispersion syndrome (PDS) is a relatively common and usually underdiagnosed phenomenon produced by spontaneous release of pigment from the iris into the anterior segment. PDS can cause pigment-related ocular hypertension (POHT) or pigmentary glaucoma (PG). Therefore, early detection and understanding of the pathogenesis are of relevance for establishing adequate therapy to prevent vision loss.

In pigment dispersion syndrome, symptoms may be absent or vary significantly, ranging from mild redness and discomfort to severe ocular pain, photophobia, blurred and halo vision. Exercise often triggers symptoms In young patients. Clinical signs in PDS include

- Krukenberg spindle
- Mid-peripheral iris concavity with a spoke-like 360 degree transillumination defects
- Pigment deposition on the anterior surface of the iris, especially within iris furrows or anterior lens capsule

Of note, Krukenberg spindle is not always present in PDS and is not pathognomonic of the entity. Additionally, it is crucial to differentiate pigment from inflammatory cells, as this can lead to misdiagnosing PDS as acute anterior uveitis in a patient with

prominent symptoms. Inflammatory cells are generally round, bigger, and whiter, while the pigment is small, tanned-brown particles with sharper edges.

Gonioscopy and fundus examination are essential in the assessment of PDS patients. The angle is usually open, and characteristic pigment deposition is often seen in the inferior trabecular meshwork. In some cases, pigmentation of the Schwalbe line occurs, giving the appearance of a Sampaolesi line, a brown pigment at or anterior to Schwalbe line observed in PDS or pseudoexfoliation syndrome. Another important gonioscopic finding in PDS is backward-bowing of the iris.

Two entities in pigment dispersion syndrome are pigmentary ocular hypertension (POHT) and pigmentary glaucoma (PG). POHT shares the same clinical findings as PDS but with elevated IOP and is more common in males. Monitoring the IOP must be rigorous since each 1 mmHg rise above 21 mmHg increases the risk for developing PG by 1.4 times.(Siddiqui et al 2003) Symptoms include ocular pain, injection, photophobia, and halo vision. Patients may experience symptomatology during or after exercise.

PG is a form of secondary open angle glaucoma and occurs when there is structural optic nerve damage and/or visual field changes. Although PDS tends to affect men and women in almost equal numbers, as previously noted, PG development is far more common in men. A community-based retrospective study found a low risk for developing PG due to PDS with an estimated conversion rate of 10% at 5 years, increasing to 15% at 15 years. This study also demonstrated that the most important predictive factor for the conversion is an IOP >21 mmHg at the initial diagnosis. (Siddiqui et al 2003)

PG patients tend to have a more prominent Krukenberg spindle related to the pigment showers that occur while exercising. Some patients might have subacute attacks characterised by corneal edema and blurred vision. Optic nerve cupping and visual field defects point, corresponding with the anatomical damage in the retinal nerve fibre layer and ganglion cell complex, suggest diagnosis of PG. Visual field defects are also present and tend to progress unless adequate treatment controls the IOP.

The prevalence of myopia in patients with PDS ranges from 38% to 100%. Moreover, the higher the degree of myopia, the greater the risk for developing PG. The presence of POHT (IOP >21 mmHg) at the moment of PDS diagnosis is the most important risk factor for conversion to PG.(Siddiqui et al 2003)

End of answer

Question 7

What is the natural history of pigment dispersion syndrome?

Answer:
Many patients with pigment dispersion syndrome will not develop pigmentary glaucoma over the course of their lifetime. The degree of pigment dispersion does not necessarily correlate with the development of glaucoma. Patients with pigment dispersion syndrome, normal IOP and an absence of glaucomatous optic disc changes should have regular (every 1-2 years) follow-up including clinical examination, IOP measurement, disc photographs, OCT and visual field assessment. Asymmetry between the eyes is common.

A number of reports have shown that pigment dispersion decreases with age, and IOP may stabilise. Additionally, several reports have indicated that Krukenberg's spindle and trabecular pigment become less prominent with time. Some patients may be able to discontinue ocular antihypertensive therapy, however, others will require lifelong treatment.

In most normal individuals with pigmentation in the trabecular meshwork, the pigmentation is more marked in the inferior quadrant. However, in patients with pigment dispersion syndrome or pigmentary glaucoma, the pigmentation may be denser in the superior quadrant (pigment reversal). In the absence of other signs, this may indicate to the clinician that the patient has had previous episodes of active pigment dispersion.

End of answer

Question 8

What other conditions are associated with anterior segment pigment deposition?

Answer:
Several conditions can mimic or contribute to anterior segment pigment deposition, potentially leading to misdiagnosis of PDF. It is crucial to differentiate these conditions from PDS to ensure appropriate management and prevent complications.

- Intraocular inflammatory conditions: Fuchs uveitis, herpetic uveitis, Posner-Schlossman syndrome, and Vogt-Koyanagi-Harada disease. A thorough history and clinical examination will differentiate anterior uveitis from pigment dispersion syndrome.
- Conditions causing iris depigmentation and atrophy: Horner syndrome, pseudoexfoliation syndrome, trauma, and acute angle-closure glaucoma. Patients presenting with pigment in the anterior chamber should be questioned about a history of intraocular surgery or trauma (blunt or penetrating).
- Other disorders that can resemble PDS: Ring melanoma of the iris and the anterior segment. Ultrasound biomicroscopy imaging analysis is crucial to distinguish ring melanoma of the anterior chamber from PG.

In patients with dense pigment but with absent clinical findings, secondary causes of pigment liberation need to be ruled out, especially to exclude uveal melanomas, a life-threatening disease.

End of answer

Question 9

What is the role of laser peripheral iridotomy in the treatment of patients with pigment dispersion syndrome or pigmentary glaucoma?

Answer:
In pigment dispersion syndrome and pigmentary glaucoma, reverse pupillary block results from posterior bowing of the iris, causing irido-zonular contact and subsequent pigment release. This also restricts the flow of aqueous humour and disrupts aqueous fluid dynamics.

A peripheral iridotomy involves the use of a laser to create an opening in the iris to serve as an alternative channel for aqueous flow. The rationale for performing a YAG laser peripheral iridotomy is to reduce the reverse pupillary block by flattening the iris, reducing irido-zonular contact and decreasing active pigment dispersion.

There has, however, been some debate about the efficacy of peripheral iridotomies in pigment dispersion syndrome, particularly when the patient has manifest glaucoma.

A Cochrane review article analysed the results of five randomised controlled trials of YAG laser iridotomy vs no laser iridotomy in 260 eyes of 195 participants with pigment dispersion syndrome or pigmentary glaucoma. The primary outcomes were visual field progression, onset of visual field changes in patients with pigment dispersion syndrome and ocular hypertension, and mean reduction in IOP at one year. Secondary outcomes included logMAR VA at six and twelve months, change in anterior chamber depth, change in iris configuration and pigment accumulation in the anterior chamber.

The authors noted that along the continuum of pigment dispersion to pigmentary glaucoma, different pathogenic stages can be identified. In the early stages, pigment that has been dispersed obstructs the trabecular meshwork, and granules of pigment are phagocytosed by the endothelial cells of the trabecular meshwork. In the later stages of the disease the trabecular endothelial cells become overloaded with pigment and eventually die, which can result in an increase in IOP. At this point, damage is probably irreversible. The authors hypothesised that treatment with laser peripheral iridotomy may have different success rates at various stages of the disease, with the treatment likely to be more effective earlier in the disease process.

The authors found that there was a lack of high-quality evidence on the effectiveness of peripheral iridotomy in the treatment of pigment dispersion syndrome or pigmentary glaucoma.

End of answer

Question 10

How is elevated IOP managed in pigmentary glaucoma?

Answer:
Pigmentary glaucoma is treated the same way as other glaucomas, in that the primary aim of management is to reduce IOP to a level that halts or reduces damage to the optic nerve. During the active phases of pigment release, treatment may need to be more aggressive.

In the setting of diminished aqueous drainage via the trabecular meshwork pathway, prostaglandin analogues are a first-line medical therapy as they reduce IOP by increasing uveoscleral outflow. Increased iris pigmentation can occur with topical prostaglandin therapy. However, this does not lead to an increase in pigment dispersion as the iris stromal melanocytes are affected, not the iris pigmented epithelium.

Theoretically, miotic agents, including pilocarpine, are the ideal therapy for pigmentary glaucoma as they lower IOP, prevent pupil dilation and reduce posterior iris bowing. However, the side effect profile, particularly in young patients, is poor and adverse effects include accommodative spasm, increased risk of retinal detachment and cataract formation. They are therefore not used as a primary treatment in pigmentary glaucoma.

Alpha adrenergic agonists, beta adrenergic antagonists and carbonic anhydrase inhibitors may all be used in the treatment of pigmentary glaucoma, provided there are no contraindications to these agents.

Argon laser trabeculoplasty and selective laser trabeculoplasty have been shown to be effective in the treatment of patients with pigmentary glaucoma. There have been reports of markedly elevated IOP post selective laser trabeculoplasty in eyes with pigmentary glaucoma, so close post-laser observation is advised.

Some patients may require trabeculectomy surgery to control pigmentary glaucoma. In these patients, pigment deposition may be noted within the filtering bleb, however, it is not known whether this adversely affects the function of the trabeculectomy.

End of answer

References and recommended reading

Required reading

Bustamante-Arias A, Ruiz-Lozano RE, Carlos Alvarez-Guzman J, Gonzalez-Godinez S, Rodriguez-Garcia A. Pigment dispersion syndrome and its implications for glaucoma. Surv Ophthalmol. 2021 Sep-Oct;66(5):743-760. doi: 10.1016/j.survophthal.2021.01.002. Epub 2021 Jan 12. PMID: 33444629.

Recommended reading

Niyadurupola N, Broadway DC. Pigment dispersion syndrome and pigmentary glaucoma--a major review. Clinical & Experimental Ophthalmology. 2008;36(9):868-882.

Pang R, Labisi SA, Wang N. Pigment dispersion syndrome and pigmentary glaucoma: overview and racial disparities. Graefes Arch Clin Exp Ophthalmol. 2023 Mar;261(3):601-614. doi: 10.1007/s00417-022-05817-0. Epub 2022 Sep 10. PMID: 36085315.

Siddiqui Y, Ten Hulzen RD, Cameron JD, et al. What is the risk of developing pigmentary glaucoma from pigment dispersion syndrome? Am J Ophthalmol. 2003;135(6):794e9

Michelessi M, Lindsley K. Peripheral iridotomy for pigmentary glaucoma. *Cochrane Database Syst Rev.* 2016;2:CD005655.