Case 1 – Normal Tension Glaucoma

53 year old woman attends your practice for routine exam. She has no past medical history or family history of note.

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual acuity</td>
<td>6/6</td>
<td>6/6</td>
</tr>
<tr>
<td>Ishihara colour plates</td>
<td>14/14</td>
<td>14/14</td>
</tr>
<tr>
<td>Pupils</td>
<td>No RAPD</td>
<td>No RAPD</td>
</tr>
<tr>
<td>IOP</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Slit lamp examination</td>
<td>Anterior segment unremarkable</td>
<td>Anterior segment unremarkable</td>
</tr>
<tr>
<td>Gonioscopy</td>
<td>Open angles</td>
<td>Open angles</td>
</tr>
<tr>
<td>Corneal thickness</td>
<td>564 microns</td>
<td>585 microns</td>
</tr>
</tbody>
</table>

Question 1: Comment on the optic nerve appearance of each eye including the cup to disc ratio.

Right eye demonstrates some local thinning of the nerve fibre layer at the 7 to 8 o’clock position. There is an associated nerve fibre layer haemorrhage and nerve fibre layer drop out in this area.

Both optic nerve heads demonstrate a cup to disc ratio of 0.65-0.7
Both discs follow the ISNT rule. The optic discs are of average size, although the right disc looks slightly smaller than the left.

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\begin{array}{|c|c|c|}
\hline
\text{Average RNFL Thickness} & 95 \mu m & 104 \mu m \\
\text{RNFL Symmetry} & 83\% \\
\text{Rim Area} & 0.92 \text{ mm}^2 & 1.08 \text{ mm}^2 \\
\text{Disc Area} & 2.18 \text{ mm}^2 & 2.18 \text{ mm}^2 \\
\text{Average C/D Ratio} & 0.73 & 0.71 \\
\text{Vertical C/D Ratio} & 0.74 & 0.83 \\
\text{Cup Volume} & 0.502 \text{ mm}^3 & 0.461 \text{ mm}^3 \\
\hline
\end{array}
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Fig. 2. Retinal nerve fiber layer OCT scan of right and left
Question 2: Please comment on the findings of the retinal nerve fiber layer OCT scan (Fig. 2) and retinal ganglion cell layer OCT scan. (Fig. 3)

The majority of both the RNFL Quadrants and RNFL Clock Hours are depicted as green which represents a value above 5% of the distribution of normal. The left eye has a superior RNFL quadrant of white with clock hours 10 and 12 also noted to be white. This represents a value above 95% of the distribution of normal.

When assessing the absolute values of the RNFL clock hour thickness one is able to see a reduction of thickness in the right disc at the 8 o'clock position (value of 46). This is at the lowest end of the distribution of normal (lowest 1% of age-
normal values) and is significantly different from the left eye 8 o’clock position (value of 76).

The reduction in RNFL in the right eye at clock hour 8 is also demonstrated in the RNFL deviation map.

The retinal ganglion cell layer OCT measures the combined thickness of the ganglion cell layer and inner plexiform layers. It demonstrates thinning of the inferior and infero-temporal sectors of the right eye with the thickness map and deviation map also demonstrating thinning in this distribution in keeping with the distribution of thinning on OCT RNFL in the right eye.

Fig. 4. HVF 24-2 Left Eye
Question 3: Please describe the patient’s visual fields.

HVF 24-2 SITA standard for the right and left eye are both reliable with 1% false positive errors in each eye, and no fixation losses. The right visual field demonstrates a small, shallow paracentral visual field defect. The left eye HVF 24-2 has a slightly larger blind spot but is otherwise within normal limits.
Question 4: Please give you working diagnosis, with reasoning, and comment on your initial treatment for this patient.

Given the appearance of the right eye nerve fibre layer haemorrhage, thinning of the RNFL at the 8 o'clock position, normal IOP, open angles on gonioscopy, and nerve fibre bundle defects, and visual field defect correlating with optic nerve appearance it is strongly suspicious that this patient has early normal tension glaucoma in the right eye.

As there is a nerve fibre layer haemorrhage it would be prudent to start this patient on treatment to the right eye (Hysite one drop at night) with review for assessment of therapeutic efficacy in 6-8 weeks.

Question 5: Describe the role of imaging in this patient's diagnosis.

The appearance of glaucomatous change in the optic nerve head does not necessitate imaging if other features such as raised IOP, visual field changes that match the optic disc appearance, and absence of other focal afferent visual system dysfunction are present.

Neuroimaging should be undertaken in any patient suspected of having NTG with the following signs:

- Marked asymmetry of optic nerves
- Optic nerve pallor in excess of cupping
- Visual field defects not corresponding to optic nerve damage
- Unexplained visual acuity loss
- Colour vision deficit
- Atypical neurological symptoms for glaucoma
- Age less than 50 years

In patients with optic nerve head change consistent with glaucomatous damage but normal IOP, it is important to assess for additional signs. These include:

- Afferent pathway dysfunction - optic disc pallor, colour vision deficit, reduced visual acuity.
- Neurological symptoms: Multiple sclerosis, Alzheimer’s disease, Friedreich’s ataxia, and Charcot Marie Tooth type 2A may have associated optic disc changes, RNFL defects, and visual field defects.

In this patient, imaging was not undertaken despite the normal IOP as there were characteristic features of glaucoma with no features suggestive of neurological pathology.

Question 6: Please describe the significance of optic nerve head haemorrhage in patients with glaucoma.
The presence of a RNFL haemorrhage at the optic disc, also known as a Drance haemorrhage, has been classically associated with normal tension glaucoma, however, this finding can be present in any form of POAG.

The presence of an optic disc haemorrhage is a negative prognostic indicator. The Collaborative Normal Tension Glaucoma Study group found that the risk of glaucomatous visual field progression was higher in patients with optic disc haemorrhage who were not on intraocular pressure lowering therapy.

Anderson et al reported the presence of optic disc haemorrhages at the time of diagnosis of NTG as an unfavorable prognostic marker for likely visual field progression.

The Collaborative Normal Tension Glaucoma Study (CNTGS) used the presence of a disc haemorrhage as one criteria for initiation of treatment in patients with NTG.

**Question 7: Describe IOP variations in glaucoma, how such variations can be accounted for, and relevance to this patient.**

There is considerable evidence that IOP measurement may fluctuate over a 24 hour period, however, current literature is divided upon the peak IOP time.

Most IOP measurements are undertaken during office hours at a single point in a day. It is therefore possible that this measurement is not at a time of a patient's peak IOP.

Two routinely used methods of identifying IOP variations are:

1. Multiple measurements of a patient's IOP over the course of a day to give a better idea of the diurnal IOP variation. This does not include supine or night time measurements.
2. The water drinking test. The patient consumes 1 litre of water over a 15 minute period and IOP is measured at baseline and every 15 minutes for 1 hour. This method has been shown to correlate with diurnal IOP variations.

Wide diurnal variations in IOP and nocturnal IOP spikes have been correlated with normal tension glaucoma.

**Question 8: Please describe the treatment rationale for normal tension glaucoma including monitoring and follow up.**

Reduction of IOP from baseline is the mainstay of glaucoma treatment. This can be achieved by topical medications, laser procedures, or by surgery.

The Collaborative Normal Tension Glaucoma Study (CNTGS) demonstrated the benefit of IOP reduction in the treatment of patients with NTG. This study concluded that a 30% reduction from baseline IOP resulted in lower risk of
disease progression. The criteria for initiation of treatment in NTG patients in this study was: visual field or optic nerve progression, visual field loss threatening fixation, or the presence of a disc haemorrhage.

The low pressure glaucoma study was a prospective trial in which NTG patients were randomised to treatment with timolol maleate 0.5% or brimonidine tartrate 0.2%. IOP reduction was similar between the two groups, however, patients treated with brimonidine tartrate 0.2% were found to be less likely to have visual field progression compared to the patients treated with timolol maleate 0.5%. It is unclear if this difference was the result of a detrimental vascular effect of timolol or of a neuroprotective effect of brimonidine.

Typical first line treatment in glaucoma patients is a prostaglandin drop as they have once daily dosing with systemic side effects rarely occurring. Medical treatment must be tailored to individual patients and their IOP response. Once treatment is initiated (an initial target pressure of 30% reduction from baseline IOP is commonly set), patients should be reviewed in 6-8 weeks to ensure adequate IOP lowering control and minimal side effects. Once satisfactory IOP control has been achieved patients can be monitored every 3-4 months to assess maintenance of IOP and absence of progression. If stable, patients commonly undergo optic disc assessment and HVF testing every 6-12 months.

**Question 9: Comment on the prognosis of a patient with normal tension glaucoma.**

All forms of glaucoma, including NTG, can progress to irreversible blindness. The CNTGS study demonstrated that 65% of untreated patients with NTG did not progress. However an IOP reduction of 30% with IOP lowering treatment reduced the likelihood of progression to 12%.

References:

6. Quaranta L, Katsanos A, Riva I, et al. Twenty-four-hour intraocular pressure and ocular perfusion pressure characteristics in newly

**Case 1 Test**

**Question 1:** Normal tension glaucoma is characterised by the following:

a. IOP equal to or less than 21mmHg  
b. Optic nerve damage in glaucomatous pattern  
c. Open anterior chamber angle  
d. No features of secondary glaucoma or a non-glaucomatous cause for optic neuropathy  
e. All of the above

**Question 2:** According to the Collaborative Normal Tension Glaucoma Study what percentage of IOP reduction should be aimed for in a patient with NTG?

a. 10%  
b. 15%  
c. 20%  
d. 25%  
e. 30%

**Question 3:** Select the following statement that is true of normal tension glaucoma:

a. NTG is considered to be a distinct clinical entity  
b. NTG is considered to be on a continuum of open angle glaucoma  
c. Patients with NTG will have one of migraines, Raynaud’s phenomenon, or nocturnal hypotension  
d. A patient with NTG by definition must have an IOP that does not exceed 20mmHg at any point  
e. The treatment aims of NTG vary from those of POAG

**Question 4:** Optic disc haemorrhage in glaucoma may be associated with:

a. Focal neuroretinal rim thinning  
b. RNFL thinning on OCT  
c. A corresponding visual field defect  
d. Beta zone peripapillary atrophy  
e. All of the above
Question 5: The ganglion cell complex is not affected in NTG. True or False?

Question 6: The location of an optic disc haemorrhage in glaucoma is the:
   a. Choroid
   b. Internal limiting membrane
   c. Photoreceptor layer
   d. Outer nuclear layer
   e. Retinal nerve fibre layer

Question 7: Which of the following findings would require neuroimaging for a patient suspected of having NTG?
   a. Temporal pallor of the optic disc
   b. Ophthalmoplegia
   c. Inferior neuroretinal rim thinning
   d. Optic disc haemorrhage
   e. Altitudinal visual field defect with a chalky white appearance of the optic nerve nerve head

Question 8: Clinicians may not detect peak IOP measurements on a routine glaucoma assessment due to?
   a. IOP is not measured in a supine position
   b. Most measurements of IOP occur during office hours. A patient's peak IOP may occur outside of these hours
   c. IOP measurement is a value for one point in time and may not represent a patient's IOP variation.
   d. Routine use of the IOP water drinking test is not common
   e. All of the above

Question 9: The water drinking test:
   a. May help identify IOP peaks
   b. Involves a patient consuming 1 litre of water prior to a single IOP measurement
   c. Is performed over 15 minutes
   d. May be undertaken on all patients without any risk
   e. Is performed in a supine position

Question 10: Patients with NTG have a higher rate of disc haemorrhages compared to POAG. True or False?

Question 11: Which of the following statements about the Collaborative Normal Tension Glaucoma Study is false?
   a. Optic disc haemorrhage presence was not an end point in this study
   b. Patients with NTG that were treated were 23% more likely not to have progression compared to untreated NTG patients
c. The majority of patients in the untreated group demonstrated progression at three years.
d. 12% of treated eyes were deemed to have progression.
e. IOP reduction reduces the risk of NTG progression.

Question 12: The Collaborative Normal Tension Glaucoma Study identified the following as risk factors for glaucoma progression:

a. Optic disc haemorrhage at presentation
b. Migraines
c. A and B
d. Female gender
e. A, B, and D

Question 13: What class of medication is Timolol?

a. Carbonic anhydrase inhibitor
b. Alpha 1 adrenergic agonist
c. Prostaglandin analogue
d. Alpha 2 adrenergic agonist
e. Beta blocker

Question 14: What class of medication is brimonidine?

a. Carbonic anhydrase inhibitor
b. Miotics
c. Prostaglandin analogue
d. Alpha 2 adrenergic agonist
e. Beta blocker

Question 15: Patients with POAG have higher rates of notching compared to NTG. True or False?

Question 16: The aim of treatment in NTG is:

a. To lower IOP by 20% or less
b. To reduce IOP to under 9mmHg
c. To reduce IOP to as low a value as possible
d. To lower IOP using multiple medications as there is evidence to suggest that some have additional IOP independent factors
e. To lower IOP by 30% from baseline

Question 17: You have just diagnosed a patient with NTG and commenced a topical IOP lowering medication. Which of the following would be most appropriate for this patient’s next follow up appointment?

a. 6 months with IOP check, HVF 24-2 and optic disc exam to assess for progression
b. 3 months with IOP check, HVF 24-2, and optic disc exam to assess for progression
c. 2 weeks for IOP check
d. 2 months for IOP check
e. C and B

Question 18: Which of the following are potential differential diagnoses for NTG?

a. Intermittent angle closure glaucoma
b. Myopia with peripapillary atrophy
c. Optic nerve coloboma or optic nerve pits
d. Posner-Schlossman syndrome
e. All of the above

Question 19: The following is not an indication for imaging in a patient suspected of having NTG:

a. Marked asymmetry of the optic nerves
b. Unilateral temporal neuroretinal rim thinning
c. Colour vision deficit
d. Visual field defects not corresponding to optic nerve damage
e. Optic nerve pallor in excess of cupping

Question 20: The indication for surgical intervention in NTG is based upon peak IOP measurements at 6 and 12 months whilst on medical treatment. True or False?

Question 21: The following feature(s) is/are seen characteristically in NTG and POAG:

a. Optic disc haemorrhages
b. Notching
c. Peripapillary atrophy
d. A and B
e. A, B, and C

Question 22: Which of the following adverse effects is not associated with brimonidine?

a. Conjunctival hyperaemia
b. Conjunctival follicles
c. Dry mouth
d. Daytime sleepiness
e. Nightmares

Question 23: The following is false for visual field changes in patients with NTG:

a. Visual field changes in NTG are almost exclusively arcuate scotomas
b. Defects tend to be more focal and occur closer to fixation early in the disease

c. Nasal steps may be seen
d. A and C
e. B and C

Question 24: The Collaborative Normal Tension Glaucoma Study demonstrated:

a. 35% of untreated NTG patients progressed
b. 16% of treated NTG patients progressed
c. No significant reduction in progression was seen between treated and untreated groups
d. A and B
e. B and C

Question 25: All patients with NTG require neuroimaging to exclude a compressive lesion. True or False?