To Treat, or Not to Treat - A Dilemma in Glaucoma

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To treat or not to treat – a dilemma

Glaucoma undoubtedly is the leading cause of irreversible blindness. The population of human beings predicted to be diagnosed with glaucoma is reaching alarming proportions. It is estimated that there will be 60.5 million people affected by the year 2010 and increasing to almost 80 million in the next decade 1. Not surprising, since over 90% of recently detected glaucoma patients were unaware of their condition 2.

The results of the various randomized controlled trials 3,4 have proved that initiation of appropriate therapy at an appropriate time contributes significantly to retarding the progression of the disease process.

The following case is presented here since the family history of glaucoma is a significant risk factor that contributes to development of disease in a hitherto unaffected individual. Poor compliance is a part of glaucoma management due to the asymptomatic nature of disease and unrealistic patient expectation. This family perhaps represents a group of patients most glaucomatologists will encounter at some point in their practice.

Background:

A 37 year old male patient walked into our glaucoma clinic requesting an evaluation for glaucoma. He worked in a remote area in Saudi Arabia and had returned home on leave, only to find that both his parents had been diagnosed with glaucoma recently. His parents had been told about the hereditary nature of the disease and they had advised him to get screened. He decided to get himself evaluated in his home town since the place he was working did not have sufficient health care facilities and leave was available only once in two years.

Examination findings:

**Patient 1: SON, 37 years. No known ophthalmic or systemic disorders till date.**
- Visual acuity – 6/6 & N6, unaided (OU)
- Anterior segment – unremarkable
- Fundus – Average size disc with asymmetrical cupping; CDR – 0.65 – 0.7 (OD) & 0.45 – 0.5 (OS) (Figure 1: Composite ONH recording)
- Baseline IOP (GAT) – 17 mm Hg (OD) & 15 mm Hg (OS)
- Gonioscopy – open angles
- Standard white-on-white automated perimetry – Normal VF (OU)
- Nerve fiber layer thickness assessment by OCT – reported as borderline (Figure 2: HRT)

**Patient 2: FATHER, 70 years. On treatment for COPD since 20 years.**
- Visual acuity – BCVA 6/9 & N6

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1 Sundaram Eye Foundation, Chennai 2 Little Flower Hospital, Angamaly,
3 Sankara Nethralaya, Chennai, 4 Girishar Eye Hospital, Cochin, 5 Suraj Eye Institute, Nagpur 6 Adithya Khan Eye Hospital, Palakkad
Anterior segment – Grade 2 nuclear sclerosis
Fundus – Average size disc; CDR – 0.6 (OD) & 0.75 – 0.8 with inferior polar notch (OS) (Figure 1: Composite ONH recording)
Baseline IOP (GAT) – 18 mm Hg (OD) & 19 mm Hg (OS)
Gonioscopy – open angles
Standard white-on-white automated perimetry – Generalized threshold depression (OU) with significant superior arcuate defect (OS) (Figure 3)
Medication – Brimonidine 0.2% twice daily
IOP with medication – 15 mm Hg (OU)

Patient 3: Mother, 56 years. On treatment for hypertension since 5 years.
Visual acuity – BCVA 6/9 & N6
Anterior segment – AC shallow; Grade 1 nuclear sclerosis
Fundus – Average size disc; CDR – 0.75 (OD) & 0.8 (OS) with inferior polar notch and RNFL defect inferiorly (OU) (Figure 1: Composite ONH recording)
Baseline IOP (GAT) – 22 mm Hg (OU)
Gonioscopy – narrow angles widening on indentation
Standard white-on-white automated perimetry – Superior arcuate defect (OU) (Figure 4 & 5)
Medication – Latanoprost once daily at night
IOP with medication – 14 mm Hg (OU)

All patients underwent slit lamp examination, gonioscopy followed by optic nerve head (ONH)
examination using an Ocular 78D indirect lens. Detailed recording of the ONH was made including vertical disc size, rim-to-disc (RDR) ratio in all clock hours, vertical cup-to-disc ratio, disc vasculature and red free examination for RNFL defects.

Gonioscopy was done using the Sussman four mirror lens. ONH was staged using the most recent Disc Damage Likelihood Scale (DDLS) scoring. A correction factor of 1x (manufacturer’s value) was applied to the measured vertical disc diameter when assessing disc diameter.

Visual field was recorded on the OCTOPUS 301 perimeter using the G1 Dynamic program with Peritrend software (Version 6.07).
The consultants were asked to outline their strategies in managing this patient and to comment on the following points.

1. What further investigations will the "SON" require?
2. Will the HRT or GDx provide more information on the NFL?
3. Does CCT have a role in the diagnosis?
4. Since white-on-white perimetry was normal will a SWAP or Flicker perimetry throw up any early defects in this patient?
5. What are the patient’s chances of developing glaucoma?
6. If he developed glaucoma, how long might it take to cause a significant field defect?
7. Should the patient be started on medication?
8. If medication is required, what is the first choice monotherapy option?
9. What should the ideal target IOP range be?
10. How frequently will he require monitoring, especially since he lives and works in a place with inadequate eye care facilities?

**Dr. Murali Ariga**

**Summary**

This 37 year old asymptomatic male with a family history of glaucoma has IOP in the normal range (15 and 17 mmHg) with open angles and normal visual fields. Optic discs in both eyes show asymmetric cupping with no obvious neural rim abnormalities or NFL loss. DDLS has been calculated to show a score of 4 in the right eye and 3 in the left eye. Disc size in both eyes is 1.7 mm. Cirrus OCT assessment of the NFL in both eyes shows near normal measurements.

**Assessment**

I would consider that this patient has a likelihood of developing glaucoma given the fact that at least one parent has definite glaucoma in both eyes. At present however he does not seem to show any definite glaucomatous changes in either the optic disc or fields. A DDLS score of 5 or more is suggestive of an abnormal disc and it has also been stated by Spaeth that field changes are usually noted with DDLS scores of more than 5. The DDLS score may be more useful to document change or progression rather than as a one time diagnostic aid.

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**Figure 5:** Visual field of left eye of Mother
To document findings, I suggest taking good quality disc and NFL photos (preferably stereoscopic) and recording his diurnal IOP (if not feasible at least IOP recordings 2-3 times in a day both mornings and evenings). A one time central corneal thickness measurement would also be useful as baseline documentation. I would recommend a SWAP or blue on yellow perimetry if the facility is available. This is said to show up field changes almost 5 years earlier than standard perimetry. With regards to imaging there is no evidence that one technology is superior to the other in earlier detection of glaucoma. In this situation it would suffice to use any imaging technique that one has access to and do a serial exam (say every year) to detect change. The HRT appears to be the proven technology to detect such changes over time.

There is no way to exactly predict this patient’s chances of developing glaucoma. I would not treat this patient now as he does not have glaucoma at present. He would definitely require follow-up to check IOP, visual fields and if possible to image his optic nerve and NFL every 6 months.

Dr. Radharamanan

I would like to treat this 37 year old young male because,

- Very strong family history of glaucoma, both parents getting treatment for Glaucoma.
- He has asymmetry of CDR.
- Both parents come in the category of ‘Normal Tension Glaucoma’.
- He is going back to a remote place and he won’t be available for regular follow up.

A normal white on white perimetry in this patient is what prevents me from treating him. But I like to check his CCT and SWAP HRT or GDx may not be that useful in this patient. I like to record his blood pressure especially the night BP. I don’t expect an immediate field loss in this patient since both his parents had very slow defects and retain fairly good vision in 70 and 56 years. So I am for treating this man after CCT recording. If the CCT is low, I will treat him and aim to achieve minimum of 30% IOP reduction with latanoprost and if the CCT is normal range I will treat him less aggressively. I like to review him frequently but that may not be possible in this patient. But I will definitely ask him to review within one year.

Dr. Ronnie George

This is an interesting case of a 37 year old disc suspect with a family history of both primary angle closure glaucoma and open angle glaucoma. There is also a not uncommon social problem with inability to have a regular follow up.

Based on the clinical records available I would classify the Son as a disc suspect, on the DDLS the inferior neuro-retinal rim in both eyes is equal to or thinner than the superior NRR (the left more than the right) in the presence of a vertical cup-disc ratio of 0.65-0.7 in the right eye and 0.45-0.5 in the left eyes. The combination of an increased cup to disc ratio with a 0.2:1 CDR asymmetry between the two eyes needs further evaluation. The IOP (uncorrected for CCT) is normal and white on white perimetry is also normal. The OCT images are essentially normal. The dip in the TSNIT graph seen in both eyes in the superior region is probably related to the retinal vessels and not a localized NFL loss.

This person would require periodic follow up for the rest of his life and additional baseline measurements, if available, would be helpful. These would include, measurement of the central corneal thickness in both eyes and daytime diurnal measurements of IOP would rule out large fluctuations in IOP. HRT measurements of the disc would be useful for follow up since the maximum progression data is available with this instrument. A baseline stereoscopic optic disc photo is a reasonable, easily available substitute (Ideally a stereo-pair of 20 degree disc centered colour photographs and a stereo pair of red free disc centered 30 or 50 degree NFL images).

SWAP would be helpful in this case, a negative test practically rules out the development of a white on white defect in the next 2 years. I would, however, hesitate to start treatment based on only a SWAP defect since the optic disc is only marginally abnormal and IOP’s are statistically normal. Glaucoma is a very slowly progressive disease with the average rate of progression is estimated to be approximately a mean deviation loss of 1dB per year after onset of disease. Even if this patient had pre–perimetric glaucoma a two year delay in
starting treatment is unlikely to result in significant visual field loss.

The family history of glaucoma needs to be taken into account, the lifetime risk of POAG a family member has been estimated to be 22%, a recent report suggests that it may be higher. There is no information about the heritability of angle closure disease. However, since parameters such as anterior chamber depth and angle width show high heritability it is likely that the risk of angle closure glaucoma in family members is higher than in others. The total risk of a family history of glaucoma (combination of angle closure disease in one parent and POAG in the other parent) is likely to be the additive risk for both together. It is unlikely to be any higher because both are probably mediated by different genetic variation.

It is necessary to explain the nature of the disease, the potential risk of glaucoma and the need for follow up to the patient. I would not advise any medications in this case since there is no evidence of perimetric disease at the present and IOP's are in the mid range. In ideal circumstances a review after 6 months would be appropriate. If all other investigations (SWAP, CCT) are normal, the risk of progression in 2 years is minimal.

5. **Chances of developing Glaucoma?**
   The risk factors are pretty high. Both parents have typical glaucomatous field changes. The patient himself has asymmetry in CDR. But I am unable to mention any percentage of risk.

6. **When will he develop field defects?**
   Studies show that field defects appear a few years after typical RNFL changes in one of the pre perimetric machines. Here OCT RNFL is normal. So my guess is that he is not going to develop any significant field loss for 5 – 6 years.

7. **Should medication be started?**
   I wouldn’t start treatment for the son with the available data. His risk increases if the corneal thickness is less than 490. Even if that is the situation I would prefer to wait. No catastrophe is going to happen in 2 years. If, during his next visit to India, he develops any pre perimetric change, then treatment can be started.

8. **Choice of drug**
   My first choice would be a PG analogue. This gives a substantial reduction of IOP. Considering his age, we should aim at a target of 10 to 12.

9. **Follow up**
   There is no doubt that he requires close follow up. Even if Perimetry or OCT may not be available, a proper examination of the optic disc can be done by his local Ophthalmologist. Methods like Disc Damage Likelihood Scale comes in very handy in such situations.

**Dr. Vinay Nangia**

1. **What further investigation will the patient require?**
   I feel all the relevant investigations have been done. Probably a CCT and diurnal variation will throw some additional light on the clinical scenario.

2. **Will the HRT or GDx provide more information?**
   A composite printout of OCT plus GDx is already provided. Looks like a reliable and good printout with just a bit of nasal thinning in the left eye. I don’t think an HRT will give any additional information.

3. **Does CCT have a role in the diagnosis?**
   A CCT should definitely be done, not to diagnose Ocular Hypertension, but to look for a thin cornea, something less than 500, which will definitely add to the risk of development of glaucoma in future.

4. **Will SWAP or Flicker show any defects?**
   With almost no RNFL defects in OCT, I don’t think any other Perimetry will show any additional field defect.
this by itself may not be sufficient to determine whether one may wish to label the son as having glaucoma, indicating thereby that therapy for glaucoma be started.

Visual evaluation of the retinal nerve fiber layer along with HRT data may strengthen the clinical evaluation and impression.

3. Does CCT have a role in the diagnosis?

Ans: CCT ought to be done in this situation, since he is a glaucoma suspect. A lower CCT may explaining a lower IOP. This would indicate an even greater need for detailed follow up, Since subjects with lower CCT are known to present with greater amount of visual field loss because of the lower IOP measurements.

4. Since white-on-white perimetry was normal will a SWAP or Flicker perimetry throw up any early defects in this patient?

Ans: A SWAP may be done and the possibility exists that an early defect may show up, keeping in mind the obvious asymmetry between the two eyes.

5. What are the patient’s chances of developing glaucoma?

Ans: Family history is always important and taken into consideration. He has a higher chance than normal of developing glaucoma.

6. If he developed glaucoma, how long might it take to cause a significant field defect?

Ans: There is no hard and fast rule for developing a visual field defect. One may not note a visual field defect even after losing a significant percentage of the retinal nerve fiber. I assume that a significant visual field defect is one that meets the definition of a glaucomatous visual field defect. If this patient had retinal nerve fiber layer changes in association with the obvious optic disc asymmetry, then even with the earliest consistent visual field change (even one that does not meet the classic criteria of a visual field defect) one may consider labeling a patient as having glaucoma.

7. Should the patient be started on medication?

Answer: For the time being, he ought to be followed up. A threshold of glaucoma diagnosis is needed to start a person on antiglaucoma therapy, which is for life.

8. If medication is required, what is the first choice monotherapy option?

Answer: One may opt for prostaglandins or beta blockers with due regard to systemic factors and local acceptance.

9. What should the ideal target IOP range be?

Answer: If we assume that minimal diagnostic criteria have been met at his current IOP, then the target pressure would be in the low teens. This is a hypothetical situation and this answer must be understood in that context.

10. How frequently will he require monitoring, especially since he lives and works in a place with inadequate eye care facilities?

Answer: He may be followed up once in six months.

**Editor’s comments:**

This patient, seen in isolation, may be uninteresting to a general ophthalmologist except for the asymmetrical cupping. However, when viewed in a background with a strong family history of glaucoma it is bound to instantly draw the attention of the ophthalmologist.

**Management Plan**

When assessing this patient, equal importance has to be given to the following factors.

1. Both parents have significant glaucomatous optic neuropathy, though by different mechanisms. Heredity plays a significant role in OAG.

2. Patient is employed at a place in Saudi Arabia where monitoring facilities are not easily accessed and leave is available only once in two years.

3. Compliance is a major issue as all three members of the family are defaulters.

   - Neither have the parents returned for follow up nor did the patient come back after the OCT. (The imaging report was obtained directly from the referral center).

   - He has not come back for his CCT measurement and diurnal phasing as he has returned to his work place, cutting short his leave.

1. **Assembling the parameters**

Assuming that the patient was available for further investigation the first priority would be to measure the central corneal thickness. A thinner cornea would be an additional risk factor besides the family history and
asymmetrical cupping. A diurnal phasing, at least during the day may throw light on the fluctuation in baseline IOP. In the event of an indication for medical therapy the target range of IOP will be decided by the diurnal curve and the CCT. If possible, a SWAP or Flicker perimetry to rule out early damage (unlikely with a normal OCT) can be done.

Once that is done, the following parameters will be available.

1. Angle status
2. Base line intraocular pressures, including diurnal fluctuation
3. Central corneal thickness
4. Optic nerve head parameter
   a. Disc size
   b. Cup disc ratio
   c. Rim with in all quadrants
   d. DDLS score
5. Standard achromatic visual field
6. Nerve fiber layer status

2. Analysis and assessment

As mentioned earlier, this patient viewed in isolation, may not warrant any therapy except an annual monitoring. However, with both parents having been diagnosed with glaucoma, the patient has been subjected to a battery of tests. With the available parameters, no definite pointer is readily available to suggest initiation of therapy. Perhaps, serial fundus photos and optic nerve head parameter monitoring would have been sufficient. If the patient had been available for a diurnal phasing and CCT measurement the findings could tip the scales in favour of therapy.

3. Decision to monitor

Assuming that CCT were normal and diurnal curve did not show an IOP of more than 20 to 22 mm Hg we would not be far wrong in just monitoring him. Optic nerve head assessment and intraocular pressure monitoring every six months; annual perimetry (if required SWAP or Flicker) and nerve fiber layer analysis on HRT would be the ideal protocol. This will hold if the patient is complying with instruction for follow up. We need to keep in mind his distant work place and lack of infrastructure for proper monitoring locally.

4. Decision to treat

With a strong family history of, perhaps, late onset glaucoma of low pressure type in one parent and the relative inability of patient for follow up a less aggressive strategy maybe adopted if therapy is to be initiated. With a normal CCT we could aim for a target IOP about 20 % less than baseline. However, if the CCT is less than 480-490 microns the chances of development of significant glaucomatous damage in the patient’s life time increases and therefore we may need to be more aggressive. An IOP reduction of at least 30% from baseline should be our target.

5. Follow up & monitoring

Monitoring this patient without therapy is a tricky affair considering his inaccessible location and a query regarding compliance. The first step is to counsel the patient regarding the very real possibility of his developing the disease a few years down the line. The role of family history the predominant risk factors needs to be explained. The asymptomatic nature of the disease and its potential to cause significant irreversible damage has to be highlighted. The counseling has to also involve other family members, both those already affected and those not affected. Explaining the nature of the disease with the visual field defect of parents will emphasize the serious nature of the disease and need for regular voluntary monitoring.

One of the easiest ways to detect, assess and monitor a manifesting glaucomatous neuropathy will be the Disc Damage Likelihood Scale (DDLS). It is a simple but versatile tool that needs only clinical skills and minimal instrumentation. The first clue to progression lies in the narrowing of the rim and appearance of nerve fiber layer defects. Most optic nerve head parameters can be monitored with the DDLS and its sensitivity and specificity has been proven to as good as any imaging device. If the patient is accessible this can be done every six months and can substitute a fundus photograph in places without fundus camera.

Standard automated perimetry should be an annual affair interspersed with SWAP or Flicker perimetry if suspicious optic nerve head or nerve fiber layer changes are noticed. Pre-perimetric glaucoma can be detected by progression recorded by serial optic disc stereo...
photographs and DDLS. They have been proven to be more sensitive or equally sensitive to analysis by the imaging devices 7. DDLS has also been proven to correlate well with HRT and visual field defect 8.

6. Conclusion
First degree relatives of those diagnosed with OAG are 10 times more likely to develop glaucoma than those with no family history. In the Barbados Eye Study, 23% of relatives of families with glaucoma had manifest OAG at examination. We can’t be far wrong in pursuing family members of our patients diagnosed with glaucoma especially when there is evidence to show that 90% of glaucoma diagnosed in our country is accidental.

Rather than wait for a patient to walk into our offices with advanced disease, it is our responsibility to “Chase the Family” 6 and halt the relentless progression of the disease among our vastly un-informed population.

Imaging devices aid in detecting and monitoring disease but they can at best support clinical findings and cannot be the basis for therapy. Currently their availability and accessibility is limited and till such time they are freely available we need to trust our clinical and observational skills to pick up subtle changes that herald the onset and progression of this sight stealing disorder.

References
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