Case Record 9

POAG/NTG Patient

January 2012

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aaron optometrists

Glaucoma definitions: are they important?

Normal Tension Glaucoma (NTG) is often defined as a sub-group of Primary Open Angle Glaucoma (POAG) (Kroese and Burton 2003, European Glaucoma Society 2003, Royal College of Ophthalmologists 2004, Riad 2008). However, Shields, Ritch and Krupin (1996) remark that historical nomenclature reflects the incomplete understanding of the pathophysiology involved and treatment modalities should be aimed at modulating these processes. Indeed, the existence of NTG was not firmly established until the mid twentieth century (Werner 1996) and until recently strong opinion advocated that treatment would not be of help to patients with NTG (Karmel 2006).

The separation of NTG and POAG is made more problematic by the increasing understanding of the inadequacies of all clinical tonometry techniques. Central corneal thickness (CCT) is now well established as a primary confounder of IOP readings; variations from true intracameral pressures of up to 10mmHg depending on CCT have been demonstrated (Whitacre and Stein 1993, Brandt 2004).
The differential diagnosis of NTG and POAG may be clinically academic since, while multi-factorial patho-mechanisms are accepted, the only treatment is to reduce intra-ocular pressure (IOP), regardless of the initial level (EGS 2003).
However, while outflow facility is reduced in virtually all glaucomas (Toris and Camras 2007), it is near normal in NTG (Werner 1996). Further, systemic hypotension, particularly nocturnal dips, general vascular disease, vasospastic phenomena, and higher incidence of disc haemorrhages are all more prevalent with NTG (EGS 2003, Werner 1996). This varying susceptibility to different pathological mechanisms suggests that, if not separate pathological entities, the two variants may well be managed quite differently in the future.

For this patient the considered diagnosis is one of NTG once corrected for central corneal thickness (CCT).

Initial Presentation November 2010

Salient information taken from electronic records

DATE: 3/9/10

Mrs Age : 72.
Address

Presenting Symptoms
Routine check. VA down a little – aware of cataracts. No diplopia. No HAs.

POH
Varifocals. Aware if cataracts.
No previous history of general or ocular medication use or surgery.

FOH
None

General Health and Medications
No Medicaltions, general health excellent.
Allergic to nickel. No Hayfever
BP normal. Recent blood screen normal
No Headache history
Non-Smoker

Refraction
R -3.00/-3.00X100 (6/9.5) Add +2.25 N5
L -5.25/-3.00 x80 (6/7.6) Add +2.50 N5
Phorias Dist- 8Eso 1RH Near 2Exo Dist Mallett – 4Out

Tensions (GAT) (12.42pm) R 18 L 18
(11.00 am) R 17 L 19

Glaucoma Fast Threshold Attached

GDx Attached

Pachymetry 545µm 557µm
Pupils E&A D,C& N

Slit Lamp

VH 4+ Angles open, Iris configuration Concave. Corneas clear, no pigment, Iris clear.

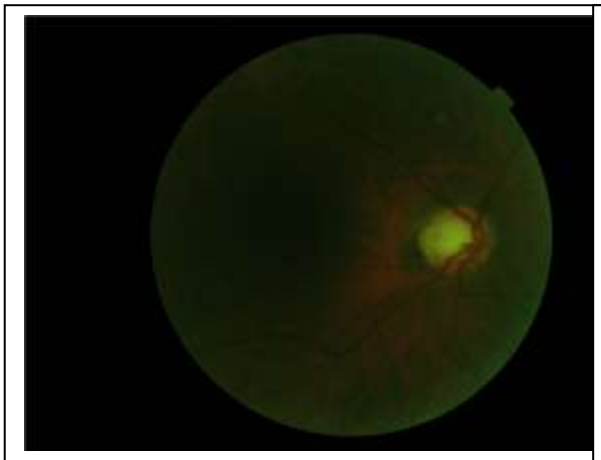
Dilated Fundsocopy (0.5% Tropicamide) Right

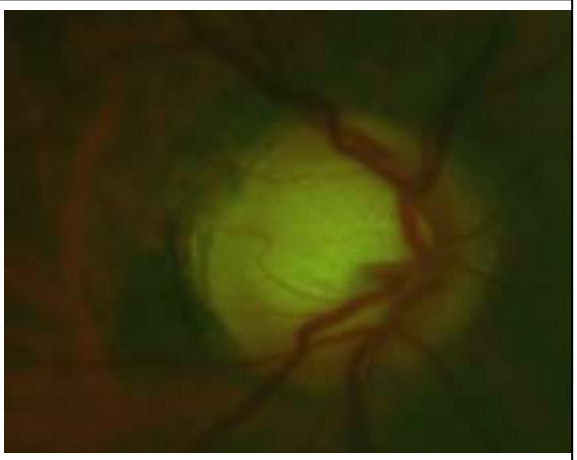
Circumferential PPA. Greater Temporal Crescent

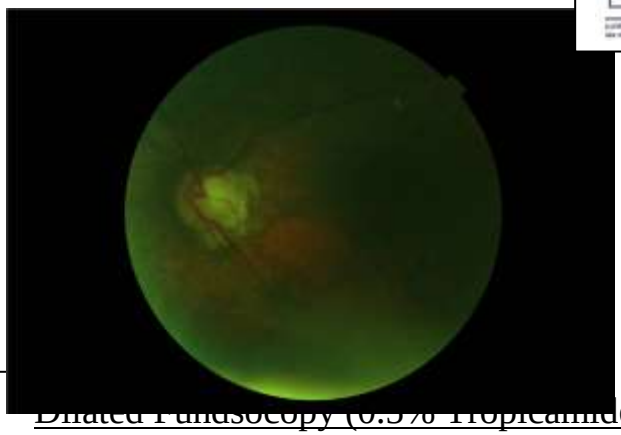
VCD 0.7 with Prominent Lamina Cribosa with nasal placement of vessels

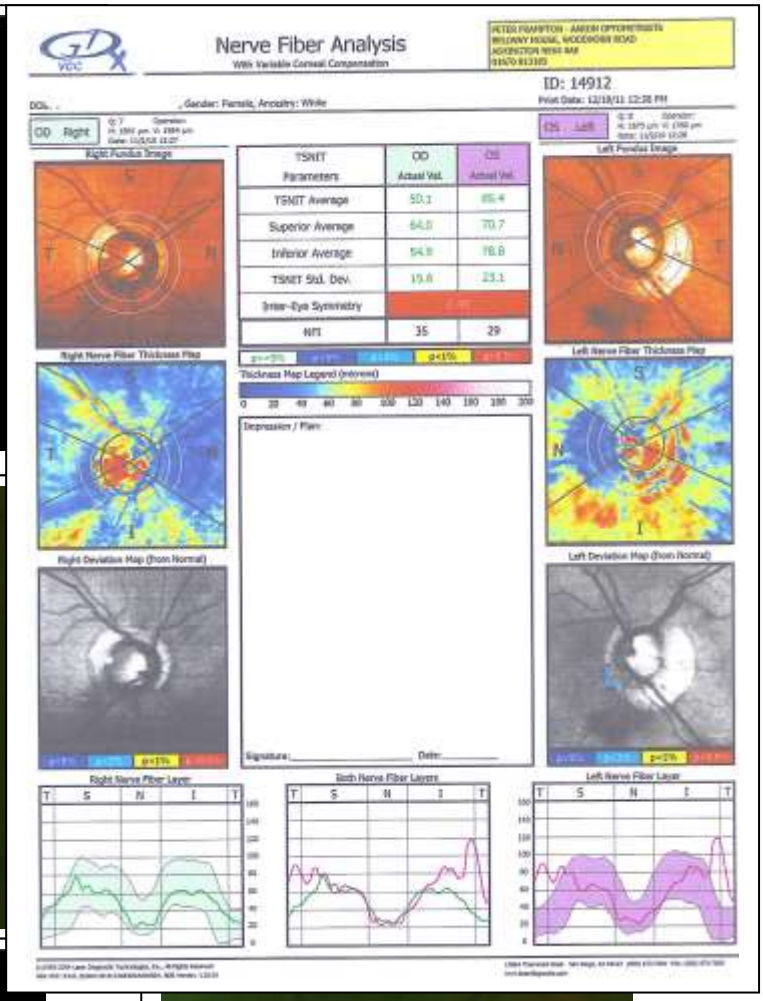
Possible baring of inferior Circumlinear vessel

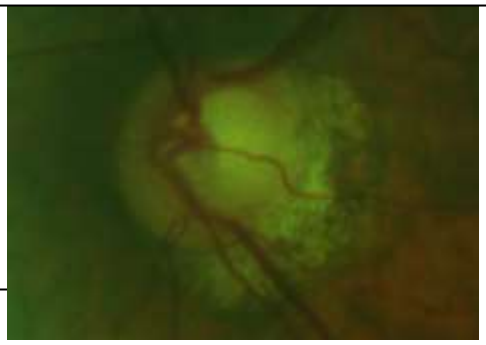
No RNFL defects noted





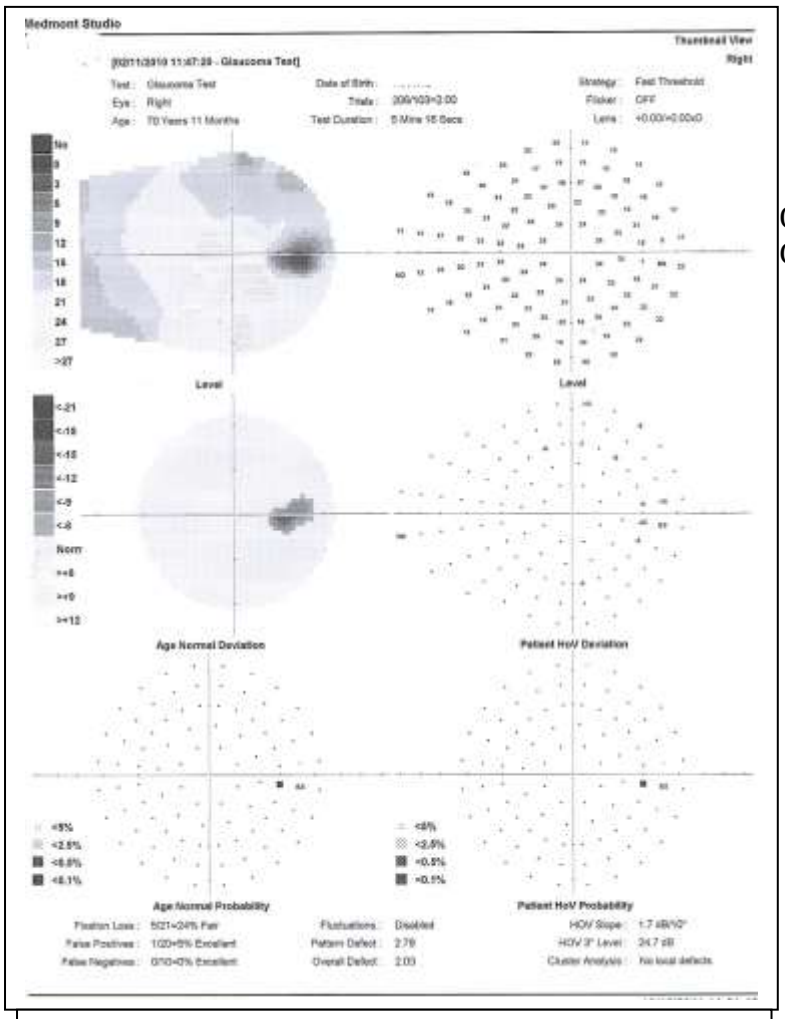






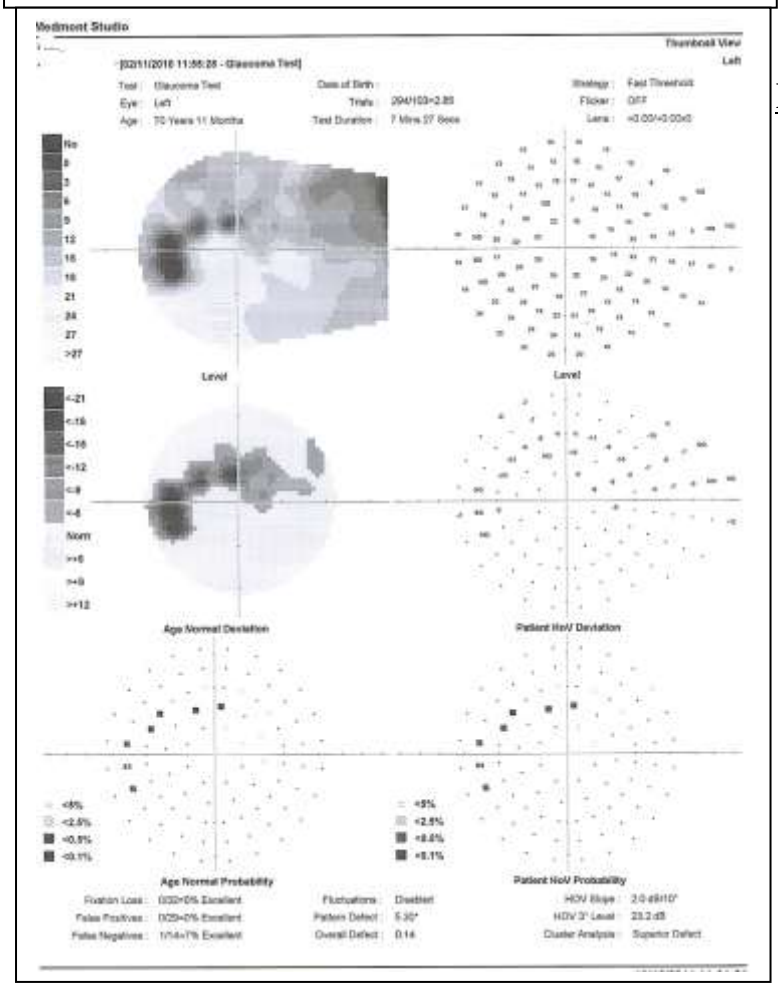
Dilated Fundsocopy (0.5% Tropicamide) Left

Circumferential PPA. Significant PPA Temporally. VCD 0.7 with inferio/temporal thinning corresponding to PPA. Prominent Lamina Cribosa with nasal placement of vessels. No RNFL defects noted



Right Glaucoma Fast Threshold

Pattern Defect: 2.79
Overall Defect :2.03
Cluster analysis : No Local Defects
Reliability Indices : Excellent



Left Glaucoma Fast Threshold

Pattern Defect : 5.30*
Overall Defect : 0.14
Cluster analysis : Superior Defect
Reliability Indices : Excellent

At this routine examination the initial history did not suggest points of concern. General health was excellent with no current medical conditions requiring treatment or any significant past medical problems, including headaches or past steroid use.

Tensions were recorded with GAT at 18mmHg. Initial slit lamp examination showed the angles to be open, cornea, iris and anterior lenses were clear. The European Glaucoma Society (2003) suggests CCT to be crucial in the initial management of ocular hypertension and remark that this parameter is of limited value for POAG. This statement presumably includes NTG, although the same paper does suggest that CCT is also important if the clinical findings do not match with IOP.

It was not until disc assessment that re-appraisal of tensions with CCT were considered. The left disc in particular showed thinning of the inferior rim with associated peripapillary atrophy. The right showed possible barring of the inferior circumlinear vessel.
The GDx NFI figure was outside normal limits for the right eye and on the limit for the left (Laser Diagnostic Technologies 2004). Relying purely on statistical comparisons to normals can be unsatisfactory without clinical appraisal. The PPA is too large to make the NFI reliable; what is interesting in the print out is how well the inferior neural rim thinning is visible compared to the digital photograph.
The superior arcuate field loss corresponded to this inferior neural rim thinning. The reliability indices were excellent; as important the field loss was characteristic of the disc damage noted (Anderson 1992). Repeating fields for confirmation is advocated to reduce false positive referrals (EGS 2003). This was not considered in this case; the disc appearance was extremely suggestive of glaucoma and correlated to the arcuate scotoma.
Repeating tensions and correcting this for CCT was considered important. Brandt (2004) reports a correction factor of 7mmHg per 100µm, with a zero correction required with CCT of 520µm (Ehlers and Hansen 1974). Tensions were confirmed to be in the normal range; with CCT of 545 and 557µm, the diagnosis of NTG was not modified to one of POAG.

The decision to refer for an Ophthalmologist's opinion was taken.

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INDEPENDENT
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Dr
Coquet Medical Group
Hadston

re Mrs DOB

6/11/10

Dear Dr

I examined Mrs routinely on the 2nd November. Refraction gave:

R -3.00/-3.00x100 (6/9.5) Add +2.25 N5
L -5.25/-3.00x80 (6/9.5) Add +2.25 N5

Tensions were recorded as 18mmHg R & L and were repeated today to confirm. Corneal thickness was R 545nm L 557.
While tensions are within the traditional normal range there is inferior thinning of the inferior neural rim of the left disc which corresponds to a superior arcuate field loss (attached).

Drainage angles are open.

Mrs requires referral for full glaucoma assessment.

Yours faithfully

Peter Frampton

Ophthalmology Assessment and Latanoprost.

Heijl et al (2002) consider it appropriate to monitor some patients, although this must depend on individual risk factors. Classically not in a high risk group based on age, IOP, FHG, asymmetric cups, the scotoma in the left eye is close to fixation and the consultant instigated treatment with Xalatan® nocte.

The NICE guidelines (2009) suggest for this age group prostaglandin analogues as first line treatment; pro-inflammatory mediators increasing uveoscleral outflow (Camras 1996b).

Prostaglandins demonstrate equal (Watson and Stjernschantz 1996) or superior (Camras 1996a, Camras 1996b) hypotensive effects compared to the β-Blocker Timolol, require single daily administration (Phelan 2002) so aiding compliance (Watson 1998), and show very few serious side effects (BNF 2011, Camras 1996b).
Common undesirable effects include inceased iris pigmentation, mild to moderate conjunctival hyperaemia and transient punctate epithelial erosions (Camras 1996b, electonic medicines compendium 2011).
A more serious side effect of prostaglandins, due to their pro-inflammatory nature, is to exacerate asthma, iritis, uveitis and local oedema (emc 2011, Camras 1996b, BNF 2011). At the concentrations stipulated these effects have not been found to be clinically significant (Watson and Stjernschantz 1996).
This point, however, stresses the increasing need for optometrists, if they wish to become members of clinical management networks, to pro-actively glean a full medical history and collate medications meaningfully. The NICE guidelines (2009) specifically state that knowledge of current systemic and topical medications and drug allergies and intolerances are vital to the correct management of a patient. These must become standard enquiries with all patients presenting for examination.

The patient did not report any cardiovascular or pulmonary health problems and had not undergone any intra-ocular surgery and did not report a past history of ocular disease or inflammation. Regardless, non-selective β-blockers are known to cause cardiovascular and pulmonary side effects (BNF 2011, Camras 1996a, Geiser, Juzych, Robin and Schwartz 1996), the safer systemic side effect profile of Prostaglandins and the lack of more specific contra-indications for this patient would justify the initial choice of Xalatan®.

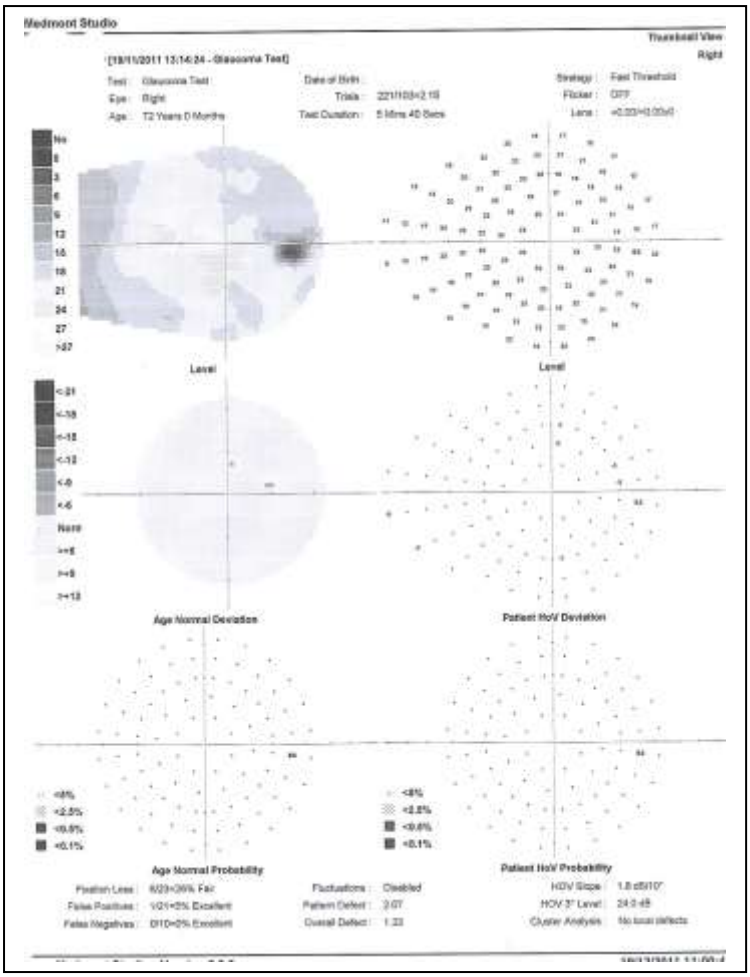
The SPC for Xalatan® (emc) recommends one drop in the affected eye(s) once daily and suggests the optimal effect is obtained with evening administration. The pivotal paper by Alm and Stjernschantz (1995) did report that evening administration was more efficacious in lowering IOP than morning dosing. However, the authors report maximal drug effect after 12 hours; their choice of sampling times favoured evening dosage. Other papers (Kiuchi, Takamatsu and Mishima 1994, Kontas et al 1999, Kontas et al 2002, Watson 1998) do not support the improved efficacy with evening instillation.

While the literature suggests that the maximal drug effect is after 12 hours (Alm & Villumsen 1991, Hotehama & Mishima 1993, Hotehama *et al* 1993, Kontas *et al* 1999, Villumsen & Alm 1992), twice daily administration does not show an increased hypotensive effect. The SPC for Xalatan® (emc 2011) specifically states that 'dosage should not exceed once daily since it has been shown that more frequent administration decreases the intraocular pressure lowering effect'. Camras (1996b) reported higher dosing induced an increase in intraocular tension, while Linden and Alm (2001) as well as finding no benefit with increased administration reported more inflammatory side effects. The very low concentrations, 0.005% for Latanoprost (BNF 2011) and single daily administration mirror the very fine balance required for optimal effect (Camras 1996b).

November 2011.

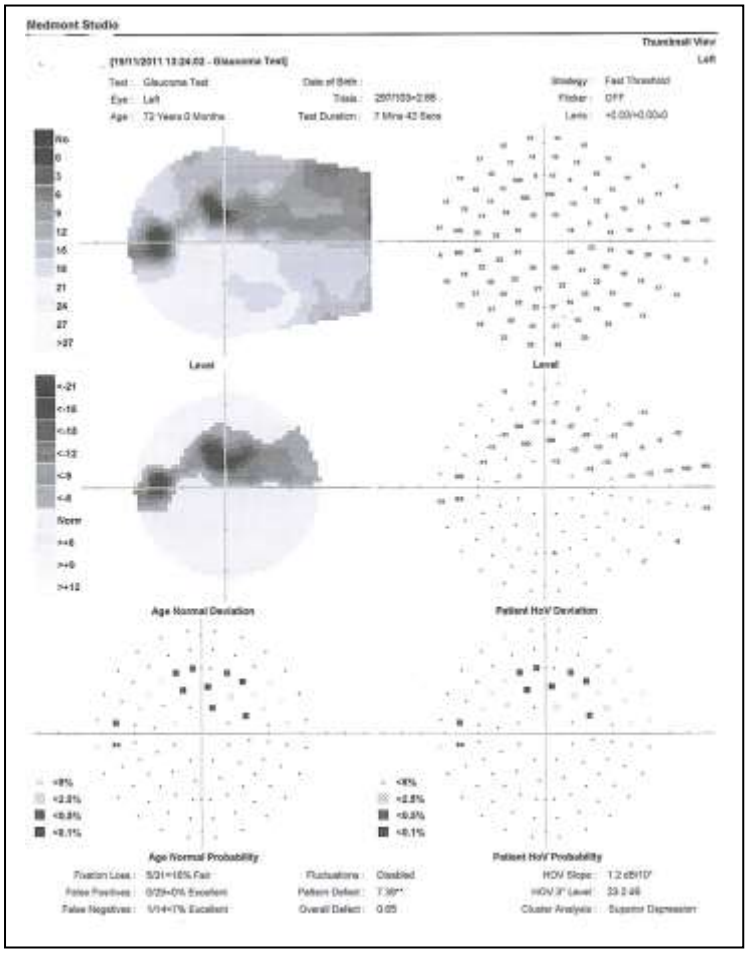
Tensions were R 14, L 13mmHg. Since her referral she has been reviewed by ophthalmology, initially at six weeks and then every three months.

The single field conducted during our review would suggest progression since referral. Cluster analysis is classified as Superior Depression and Pattern Defect is 7.39**, while the HoV Deviation shows both increased area and depth of the scotoma. Anderson (1992) suggests that assessing a VF progression from a single plot is almost impossible. Wilson (2002), European Glaucoma Society (2003) and the Royal College of Ophthalmologists (2004) suggest that identifying visual field progression requires a series of up to 6 fields.



Right Glaucoma Fast

Pattern Defect: 2.07
Overall Defect :1.22
Cluster analysis : No Local Defects.
Reliability Indices : Excelleny



Left Glaucoma Fast Threshold

Pattern Defect : 7.39**
Overall Defect : 0.65
Cluster analysis : Superior Depression
Reliability Indices : Excellent

The European Glaucoma Society (2003) gives guidance on evaluating field progression. For expansion of a pre-existing scotoma into contiguous points : ‘at least two previously normal points within 15° of fixation depressed at a p<5% level compared to baseline’ and for deepening of a pre-existing scotoma : ‘a cluster of 3 non-edge points that are part of an existing scotoma each of which worsens by at least 5dB and is depressed compared to baseline at a p<5% level on 2 consecutive fields’
The HES base progression on their own baseline, post treatment commencement. The European Glaucoma Society (2003) also stress that progression must be confirmed, while Anderson (1992) emphasises that VF variability can be a function of disease state.

Target pressures are also subjective. It is very difficult, in practice, to determine an individualised target pressure for every patient. Zeyen (1999) and the European Glaucoma Society (2003) present models for target IOP estimation, listing a number of difficult to quantify variables. The Royal College of Ophthalmologists (2004) acknowledge that the final acceptable IOP may not necessarily be the target IOP.
The Collaborative Normal-Tension Glaucoma Study Group (1998a) demonstrated categorically that a 30% reduction in IOP slowed the rate of VF progression. However the same group (1998b) report that progression still occurred in a proportion of patients regardless of this level of IOP control, suggesting either the need for greater IOP reduction for these patients or the presence of other pathogenic factors.

The proximity of the scotoma to fixation demanded a more aggressive target goal. A 30% reduction in IOP from the initial referral has been attained. If progression is considered, then the target pressure may be re-evaluated and other factors such as systemic hypotension, non-compliance or IOP spikes will be investigated.
It may be difficult medically to lower IOP more significantly. From personal communication, if the initial drug has met target but progression is still evident then, rather than replacing the effective drug, adjunctive therapy is commenced. Considering NTG, choice of an additional drug would ideally avoid medications with vaso-constrictive or systemic hypotensive effects (EGS 2003).
In this case the prostaglandin has produced a good response so the addition of a carbonic anhydrase inhibitor is often considered. Trusopt does not have systemic hypotensive effects and its primary indication is for adjunctive therapy (emc 2011). Carbonic anhydrase is an enzyme found in many tissues including red blood cells and is a sulphonamide (EGS 2011). Potential side effects, apart from sulphonamide induced IgE

mediated response, involve electrolyte imbalance; renal impairment, hyperchloraemic acidosis as well as local effects of corneal oedema and corneal erosions.

If maximal medical therapy fails to halt progression then the European Glaucoma Society list Laser Trabeculoplasty and finally Surgery in the continued management of incalcitrant NTG.

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