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Normal Tension Glaucoma
Treatment-Not so fast!

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63 year old female patient initially diagnosed with normal tension glaucoma OD and has been followed for the last 7 years with no obvious progression. Entering IOPs were OD 18 & OS 16 mmHg with no significant diurnal variation. Central corneal thickness was OD 530 and OS 550 μm. History of migraine headaches for several years, but no medications or reported drug allergies. No family history of eye disease. Slit lamp was WNL OU and gonioscopy revealed open angles. Dilated fundus exam was WNL except for a suspicious inferior temporal rim notching of the OD nerve with C/D .8/.6. The OS was WNL with a C/D .5/.5 & no Drance hemorrhages noted. Optic disc photo OD (Fig. 1) reveals inferior temporal rim thinner than superior. Humphrey visual fields (HVF) showed dense superior paracentral scotoma OD (Fig. 2); OS WNL.
Initial OCT confirmed inferior temporal (I/T) rim damage with I/T NFL loss in only this quadrant. The patient was educated regarding diagnosis of NTG OD. After a discussion of the pros and cons of treatment, the patient decided on treatment: Alphagan P q 12 h OD only. Target pressures were 10-12. Follow up IOPs were 13 mmHg OD and have remained in the 13-15 range over the years. Glaucoma progression analysis of the HFA (Fig. 3) showed little progression. Heidelberg SD-OCT shows the loss of the inferior temporal NFL in the OD with no progression. Note that an inferior temporal nerve fiber wedge defect is seen on the confocal fundus image OD (Fig. 4). Recent posterior pole retinal thickness measurements to document the ganglion cell/RNF loss that can occur in glaucoma patients, shows significant loss of the retinal thickness in an arcuate shaped area inferior temporally that extends to the macula (Fig. 5). Whether these retinal thickness changes may be an earlier marker of glaucomatous damage prior to optic nerve NFL loss is unknown. Is the stability of this NTG due to IOP lowering, neuroprotective properties of Alphagan P or a non-progressing NTG?
A 64 year old male was referred to the Advanced Ocular Care Service for NTG work up based on optic nerve head notching OD & corresponding VF defect. OS was WNL. History included cardiovascular disease, heart attack 7 years ago & retinal-vascular accident OD 6 years ago, however there were no visual complaints. BCVA OD 20/20 and OS 20/20, pupils were normal with no APD. Slit lamp revealed no secondary signs and open angles with gonioscopy. His IOPs were 17 mmHg in both eyes with central corneal thickness of 625 μm in both eyes. Dilated fundus exam did reveal obvious asymmetry of optic nerve head cupping with the inferior temporal rim thinned and notched OD. (C/D .7/.5) OS was WNL (C/D .4/.4.) (Fig. 1 & 2) & no Drance hemorrhage or obvious pallor of either optic nerve. HVF revealed a dense superior, centrocecal-like defect OD (Fig. 3) and normal OS. SD-OCT shows localized NFL thinning in the I/T quadrant OD (Fig. 4) and a large area of retinal thinning in the inferior hemisphere (Fig. 5).
These findings can be seen with optic nerve damage in NTG patients but if one performs a line scan over this area of retinal thinning we must rethink the etiology of damage. The line scan reveals loss/differentiation of NFL, GC, & Inner plexiform layers with what appears to be residual glial tissue. There is preservation of the outer nuclear, photoreceptors and RPE layers (Fig. 6), consistent with the loss of retinal tissue seen in BRAOs (see ref 7) with outer layers intact due to a normal chorioidal supply. Revised diagnosis: previous BRAO with secondary retrograde optic neuropathy and NFL defect. Management at this time is no treatment with follow-up of HVFs and SD-OCT imaging to monitor progression. No progression would confirm revised diagnosis.

Figure 5 Large area of inferior retinal thinning-OD

Figure 6 Line Scan over Retinal Thinning Area
CASE 3

25 year old Asian female presents for a second opinion regarding treatment of NTG with Lumigan in each eye for the last year. No family history of glaucoma. Medical history is significant for a diagnosis of Myasthenia Gravis with no treatment at this time. Patient reports having several MRIs, but no abnormal findings found. BCVA OD 20/20 & OS 20/20. Slit lamp was WNL with no secondary signs and open angles. There was a mild but obvious afferent pupilary defect OS. Gonioscopy was WNL. IOPs were OD 15 & OS 14. Pachymetry was OD 579 and OS 598. The dilated fundus exam revealed very suspicious optic nerve heads especially in the left eye. 78 D exam OS revealed a large C/D with suspect superior and nasal rim thinning. The OD nerve also had a large C/D but the rim appeared to be very symmetric. There were no Drance hemorrhages, disc pallor, peripapillary atrophy, pits or partial coloboma in either optic nerve. Heidelberg retinal tomography (HRT) for disc size and rim tissue revealed superior and nasal rim flagged as abnormal in the OS and the OD with suspicious rim nasally. The parapapillary NFL was also thinner superiorly (Fig. 1). SD-OCT OS revealed nasal NFL thinning with suspect thinning inferiorly (Fig. 2). Retinal thickness OS with SD-OCT revealed an atypical pattern of thinning extending from the ONH superiorly and inferiorly and the hemisphere asymmetry plot revealing greater deviation superiorly & OD reveals questionable superior retinal thinning (Fig. 3). 24-2 HVFs showed OD WNL but OS revealed an inferior nasal depression. At first this looked like a trial lens artifact but the patient has no trial lens. (Fig. 4) The VF defect was confirmed with 30-2. Tentative diagnosis was an atypical optic neuropathy.
not consistent with NTG. Previous records were requested, indicating that IOPs were 18 mmHg in each eye prior to treatment, the HVFS were very similar with no real progression and CAT scans & MRI were normal. Referral to a glaucoma specialist indicated visual field defect in OS as somewhat variable over the years but relatively consistent and stable with no evidence of a progressive optic neuropathy. Optic nerve asymmetry thought to be a congenital anomaly. Recommendation was to discontinue Lumigan with an IOP check in 1 month. If pressures are stable, follow patient with visual fields every 6-12 months. With the absence of any neurological symptoms and normal MRI results, the atypical optic neuropathy was more likely the result of a congenital optic nerve defect that should not be progressive, sparing the need for this 25 year old to be using glaucoma drops for the rest of her life.
Normal tension glaucoma (NTG) has been of great interest to the optometrist for years. NTG & POAG are not thought of as two different diseases, but a continuum of one disease with different risk factors. There is really no magic cut-off of 22mmHg. It is better to think in terms of pressure dependent and non-pressure dependent damage or combinations. We all recognize that there are often risk factors other than IOP. A few of the presumed factors for development are chronic loss of retinal ganglion cells (RGC) due to a genetic hypersensitivity to IOP, abnormal vascular factors including vasospasm (migraine, Raynaud’s), ischemia and hypertension and autoimmune diseases. Also, NTG is more likely to occur in a female, Asian patient, migraine sufferer, and a patient with obstructive sleep apnea (OSA). Several other conditions must be considered in your differential diagnosis of NTG including: very thin CCT, large diurnal IOPs, oral Beta blockers, intermittent angle closure, and a number of conditions where the IOPs were previously elevated and now have returned to normal (steroids, angle recession, pigmented, exfoliation, glaucomatocyclitic crisis). Moreover, optic nerve problems including congenital anomalies (optic nerve colobomas, pits, buried drusens), past bouts of demyelinating neuropathy, AIONs, arteriolar vascular occlusions, retrobulbar mass, and chiasmal/visual pathway lesions, i.e., one of the most important differentials is to determine if your patient’s optic neuropathy is neurological or truly NTG. Some of the key points to consider when questioning a possible neurological problem versus NTG are: is there is markedly asymmetric optic nerve disease, optic disc pallor greater than cupping, visual fields defects that don’t correspond to optic nerve head appearance, more advanced or respect the vertical meridian in VFs, a rapid progression of VFs or optic neuropathy, decreased visual acuity, color vision defects and APD. Does your patient present with any other neurological symptoms or signs? In most cases, routine CAT scan or MRI are not recommended but with any of the above factors, a scan may be necessary.

One of the most perplexing issues with NTG is treatment. Does lowering IOP in these patients have any real benefit? The Collaborative Normal-Tension Glaucoma Study (CNTGS) published in the early 2000’s, indicated that lowering IOP in these patients does help in some cases. The CNTGS found that with 30% of IOP reduction, treated patients had a 12% risk of progression versus 35% in the untreated patients over 5 years. Even though these results are somewhat convincing, a large number of untreated patients did not progress and/or were very slow in progressing. So which patients are to be treated versus careful observation? A fixation threatening VF defect, a documented progression of VFs or optic neuropathy and/or a presence of Drance hemorrhages are factors that would favor treatment. Treatment goals are a 30% IOP reduction with a target IOP of around 10-12. Prostaglandins are the most common glaucoma medication initially used. Nevertheless, it is often very difficult to achieve IOPs in a 10-12 range in NTG patients, and they often require more than one drug. Neuroprotection treatment for NTG is an ongoing discussion. Neuroprotection may offer the potential of preventing non-pressure related factors that may also be contributing to the ON damage. Although we have read for years about laboratory evidence for glaucoma neuroprotection by several drugs, the evidence from randomized clinical trials has been lacking. A recent study, the Low-pressure Glaucoma Treatment Study (LoGTS), which for some reason has not made a tremendous impact in our present treatment of NTG, has revealed some very interesting
results. The study was a randomized multicenter clinical trial of efficacy of treatment with 0.2% brimonidine versus 0.5% timolol eye drops twice a day to alter the course of low pressure glaucoma as measured by the rate of visual field progression. LoGTS revealed that there were statistically fewer brimonidine-treated patients (9, 9.1%) that had visual field progression than timolol-treated patients (31, 39.2 %). Even though we may still not really understand the reasons for these findings, a possible implication is that either Timolol drops may do something bad in these patients, or Brimonidine may have some true neuroprotective-like properties that are beneficial in the treatment of NTG. For the time being we treat most of our NTG patients with a PGA and/or Alphagan P.

REFERENCES


UPCOMING CE COURSES

November 10, 2013  Louisville Seminar
December 8, 2013  Special CE Seminar Celebrating the Career of Dr. Malinovsky
February 23, 2014  Glaucoma and Coding/Compliance Seminar
March 29-30, 2014  2nd Annual Borish Symposium

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