NORMAL TENSION GLAUCOMA

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Normal tension glaucoma (NTG) may be defined as a condition in which cupping of optic nerve head, loss of retinal nerve fiber and visual field defects similar to those seen in other forms of chronic glaucoma are seen and in which an intraocular pressure level (IOP) outside the statistically normal range without treatment has not been documented nor there is any other apparent cause for these changes.

Today the following criteria are widely used to define NTG:¹
(i) Diurnal variation of IOP for 24 hours is a prerequisite for diagnosing of NTG. A mean untreated intraocular pressure consistently equal to or less than 21 mm Hg or median intraocular pressure equal to or less than 20 mm Hg on diurnal testing, with no single measurement greater than 24 mm Hg.
(ii) Open drainage angles on gonioscopy.
(iii) Typical optic disc damage with glaucomatous cupping and loss of neuroretinal rim.
(iv) Absence of any secondary cause for a glaucomatous optic neuropathy (trauma, steroids, uveitis).
(v) Visual field defect compatible with glaucomatous cupping (disc/field correlation).
The diagnosis is therefore essentially made on the basis of optic nerve and visual field characteristics along with diurnal IOP measurements.

AETIOLOGY:
Aetiology of NTG seems to include several factors which can be divided into intraocular pressure dependent and IOP independent mechanisms. There is some evidence that IOP plays a role in the progression of visual fields in people with NTG.⁶ Mechanisms of damage independent of IOP, such as vasospasm, increased vascular resistance in the ophthalmic and central retinal artery, systemic hypotension and abnormal blood rheology may play a role.

Two of the major theories include the following:
(1) Onset of vascular dysfunction causing ischemia to the optic nerve, and
(2) Mechanical dysfunction via cribriform plate compression of the axons.

The pathogenesis of NTG is still uncertain, but recently there has been an increase interest in the vascular aetiology. Reduced ocular perfusion and hence slow ongoing chronic ischemia of the optic nerve head may give rise to pale cupped disc. Colour Doppler imaging is a non-invasive method to measure blood flow velocities (peak systolic velocity and end diastolic velocity) of the retrobulbar vessels (ophthalmic artery, the central retinal artery and vein, and the short posterior ciliary arteries). The resistive index describes the peripheral resistance to flow and its calculation is based on the two parameters of blood flow velocity.¹¹,¹²

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Clinical presentation:
The disease is frequently missed as these patients have normal intraocular pressure and often have good central visual acuity, unless the optic nerve head is carefully evaluated. A high index of suspicion is required.

OPTIC DISC
- Neural rim is significantly thinner in temporal and inferotemporal portion of disc.
- Cups of patients of NTG have sloping margin.
- Patients of NTG have significantly larger average disc area than those with chronic open angle glaucoma.
- There is higher prevalence of peripapillary haloes in eye with NTG than in eyes with ocular hypertension, suggesting that haloes correlate with optic disc damage and not intraocular pressure.
- Optic disc hemorrhages are prevalent in NTG and their presence is a risk factor for future progressive damage.

Sub groups of NTG on appearance of optic disc
a) Focal ischemic NTG is characterized by a localized defect in the neural rim, also called a polar notch, usually at the inferior pole of the disc and not usually associated with generalized concentric rim loss.

b) Senile sclerotic NTG is characterized by a pale, sloping cup with extensive, generalized rim loss and extensive areas of peripapillary retinal atrophy and choroidal sclerosis.

c) Myopic NTG features an obliquely inserted disc with a shallow cup and large, white myopic crescent.

d) Miscellaneous NTG Optic discs that did not neatly fit into any one of these categories were classified in this category.

Retinal nerve fibre layer
Nerve fibre layer defects are more localized in NTG.

Optic Disc features - Possibly more common in NTG than in high - Tension Glaucoma
- Disproportionately large amount of cupping compared to amount of visual field loss.
- More sloped, less steep neural rim edge with shallower cup.
- Preference for neural rim loss temporally and inferiorly.
- Less backward bowing of the lamina cribrosa.
- Higher than average optic disc.
- Larger than average optic disc.
- Greater frequency and extent of peripapillary atrophy and halos.
- Higher incidence of optic disc hemorrhage.
- Greater likelihood of localized defect in nerve fiber layer.

Visual fields
Visual field defects are more localized, deeper and closer to fixation.

Ocular finding associated with NTG
- Although IOP is within normal range, there is some detectable abnormality of aqueous humor dynamics.
- Patients with NTG have a higher than normal intraocular pressure response to topical corticosteroids.
- There is a significantly greater prevalence of axial myopia in patients with NTG compared with chronic OAG.

Associated systemic finding
- NTG most often is a disease of the elderly, the mean reported age in clinical studies generally is in the 60's.
- Some studies have suggested that majority of patients of NTG are females. The Beaver dam eye study found an equal prevalence in both sexes.
- Relative systemic hypotension, including postural and nocturnal hypotension are more prevalent in patient (with NTG).
- The association with peripheral and perhaps central (ocular) vasospasm and migraine and...
Raynaud’s phenomenon suggests a vascular predisposition to the condition.

**Differential Diagnosis of Normal-Tension Glaucoma**

**Undetected high-pressure glaucoma**

A. Chronic open-angle glaucoma with large diurnal pressure variation.
B. Intermittent elevation of intraocular pressure caused by another type of glaucoma.
   - Intermittent angle-closure glaucoma
   - Glaucomatocyclitic crisis
C. Previously elevated IOP
   - Steroid-induced glaucoma
   - Uveitic glaucoma
   - Burned-out glaucoma (e.g., pigmentary glaucoma)

**Nonglaucomatous optic nerve disease resembling glaucoma**

A. Congenital anomalies
B. Compressive lesions of the optic nerve and chiasm.
C. Ischemic optic neuropathy (especially arteritic)
D. Optic nerve drusen

**Diagnostic evaluation of patient with normal tension glaucoma**

**Ocular Evaluation**
- Complete ocular and systemic history
- Careful ophthalmological examination, including stereoscopic optic nerve head examination, peripheral fundus examination, gonioscopy, and perimetry
- Repeated measurement of intraocular pressure on several occasions (may include formal diurnal tension curves or home tonometry when indicated).

Patient newly diagnosed with NTG does not require a formal diurnal tension curve but, if the disease is progressing despite what appears to be adequate control of IOP then diurnal variation should be done.

**General Medical Evaluation**
- Should be tailored to individual patient; not all patients require an extensive work-up.

- Physical examination by general medical practitioner familiar with cardiovascular and neurologic disorders.
- Blood tests: complete blood count, serum chemistries, erythrocyte sedimentation rate
- Carotid flow studies when indicated.
- Neuroimaging (computed tomography or magnetic resonance imaging) when indicated.

**Indication of neuroimaging and carotid blood flow**

Routine neuroimaging of the optic nerves, chiasm, and brain in NTG is controversial. The following might be useful guidelines for obtaining neuroimaging and carotid flow studies:

1. Patients under 65 or 70 years of age.
2. Patients with an intraocular pressure consistently below 16 or 17 mmHg without treatment.
3. Patients whose visual field loss or cupping is progressing rapidly.
4. Patients with unusual visual fields or whose optic discs show excessive pallor relative to the amount of cupping.
5. Patients with markedly asymmetric disease.

**Color Doppler imaging:** is useful for measuring blood velocity and vascular resistance in ocular vessels. The most important blood vessel supplying optic nerve head is the short posterior ciliary arteries (SPCA). So the color Doppler imaging studies of SPCA are very relevant for knowing the role of ischemia in the pathogenesis of NTG.

The resistive index of the retrobulbar vessels measured by means of colour doppler imaging tends to be the most striking parameter in the assessment of disturbances in retrobulbar flow in glaucoma. Most of the studies confirm reduced end diastolic velocities associated with elevated resistive indices in the central retinal artery and the posterior ciliary arteries. Reduced peak systolic velocities of these vessels tended to be a less obvious phenomenon.

Resistive index normally is low (<0.6) in majority of normal population and NTG, however studies have shown higher RI (>0.8) in patients of NTG.
The goal in treating glaucoma is to preserve visual function. To justify the considerable risks associated with all forms of glaucoma treatment, the clinician must be reasonably certain that the disease will progress if not treated and that treatment will slow or halt this progression.

One would like to treat only those patients destined to progress.

Factors possibly associated with an increased risk of progression in patients with NTG
1. Intraocular pressure near the upper limit of normal.
2. Deep, localized notch on the optic disc rim (focal ischemic type or acquired pit).
3. An optic disc hemorrhage.
4. Low systemic blood pressure.
5. No history of hemodynamic crisis.

Treatment guidelines:
- Many patients with NTG do not show progressive loss. In these cases, treatment probably is not necessary.
- Treatment options in NTG are mainly directed towards reduction of IOP. The aim of IOP-lowering medications is for a reduction of at least 30%.
- Latanoprost has been reported on as a potential drug for achieving adequate IOP reduction in NTG. Since prostaglandins enhance ocular blood flow, latanoprost would be expected to have an additional beneficial effect with normotensive glaucoma patients having compromised ocular blood flow. The ability of β blocker to lower the IOP which is already within normal range is limited.
- ALT has been used in NTG and is sometimes effective in lowering the intraocular pressure.
- Filtering surgery should not be considered unless progressive visual field loss or progressive optic nerve cupping has been demonstrated with medication. Some authors recommend full-thickness filtering procedure, such as thermal sclerostomy, trephine, or sclerectomy, for normal-tension glaucoma.
- Medications for neuroprotection are as follows: Calcium channel blockers - Less progression Betaxolol - Improved choroidal flow, better visual field preservation Dorzolamide - Increased retinal blood flow velocity in humans Brimonidine - Increased retinal ganglion cell survival.

These agents need to be considered where an IOP reduction of 25-30% cannot be achieved, or if visual field progression continues despite it.

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