

Neurologic Evaluations in Normal-Tension Glaucoma Workups: Are they Worth the Effort?

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ABSTRACT: **Background:** Normal-tension glaucoma is a chronic progressive optic neuropathy of unknown etiology. Neuroimaging workup in these patients is controversial. **Objectives:** To determine the value of routine neurologic and neuro-ophthalmologic evaluations in patients with NTG. **Methods:** We conducted a retrospective review of all patients diagnosed with NTG in our institution between 2001 and 2006. Neurologic and neuro-ophthalmologic data were evaluated. **Results:** Sixty-eight patients were considered suitable for the study (35 males, 33 females; age range 43–90 years). Neurologic and neuro-ophthalmologic findings were normal in all of them. The computed tomography brain scan was normal in 88% and duplex carotid Doppler scan was normal in 92%. **Conclusions:** Pathologic findings in neurologic and neuro-ophthalmologic assessments were uncommon in NTG. Therefore, contrary to earlier suggestions, neurologic and neuro-ophthalmologic evaluations in typical normal-tension glaucoma patients appear to have no added value.

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Normal-tension glaucoma is a chronic progressive optic neuropathy. It is defined as a condition of optic disk cupping and visual field loss resembling that seen in other forms of chronic glaucoma, but the untreated intraocular pressure level is less than 22 mmHg and there is no known cause for these changes [1]. The diagnosis of NTG is usually established by exclusion of other optic neuropathies. The need for neuro-ophthalmologic evaluation in NTG patients is controversial [1-7]. On the one hand, compressive lesions of the anterior visual pathway can cause significant cupping of the optic nerves [8-11], in which case neuroimaging studies are recommended [12]. More recently, it was reported that 6.5% of NTG patients have clinically relevant intracranial compressive lesions involving the anterior visual pathway [11]. On the

other hand, the prevalence of abnormalities is low in patients with typical NTG and most of them do not routinely undergo neuroimaging [13,14]. A variety of factors may increase the likelihood of identifying an intracranial mass lesion in atypical cases. These factors include age younger than 50 years, lower levels of visual acuity, neuroretinal rim pallor, and poor correlation between the pattern or extent of visual field loss and optic disk cupping [13].

Because the cause of NTG is not known and in view of the controversy in the literature surrounding the need for neurologic assessment, we correlated changes detected by computed tomography and duplex carotid Doppler in patients diagnosed with NTG in order to determine the benefit of routine neurologic and neuro-ophthalmologic evaluations in the comprehensive workup of NTG patients.

PATIENTS AND METHODS

This retrospective case-control study was approved by the local institutional review board committee. NTG was diagnosed according to the glaucomatous visual fields loss, glaucomatous optic disk cupping and an IOP < 22 mmHg on diurnal curve measurements. CT results were available for 71% of the NTG patients and duplex carotid findings were available for 52%. The prevalence of pathologic findings in the neurologic examinations as well as in the neuro-ophthalmologic evaluations (visual acuity, color vision, pupil reaction), brain CTs and duplex carotid Doppler evaluations were calculated. Correlations between the duplex carotid Doppler and brain CT findings were determined by cross-tabulation, as was the correlation between the findings of neurologic examinations and brain CTs. All patients underwent visual field tests using the white-on-white full threshold or the Fastpac Humphrey 24-2 program.

The patients were divided into three groups according to the severity of disease (i.e., mild, moderate, severe visual field defects) derived from the mean deviation, pattern standard deviation, and Hodapp-Anderson-Parrish severity scores [15]. All patients underwent at least two consecutive visual field tests for evaluating their NTG severity.

NTG = normal-tension glaucoma

IOP = intraocular pressure

STATISTICAL ANALYSIS

The three groups of patients were compared for clinical parameters (pachymetry, maximal baseline IOP, IOP following treatment, and the IOP change following treatment) by a one-way analysis of variance (ANOVA). The Gabriel and the Games-Howell multiple comparison tests were used to determine significant differences between pairs of groups. This analysis was done separately for each eye. The level of significance was set at 0.05, and the SPSS for windows software, version 14.0 (Chicago, IL, USA) was used for the analysis.

RESULTS

Altogether, 33 females (49%) and 35 males (51%) in our clinic were diagnosed between 2001 and 2006 as having NTG. The mean age \pm SD of the cohort was 68 ± 11 years (range 43–90). The mean follow-up was 4.6 years (range 2.4–6.6). The mean treated IOP was 12.8 ± 2.6 mmHg (range 7–19 mmHg) and the mean IOP max was 18.3 ± 3.0 mmHg (range 10–21). They all had NTG in both eyes but with different severity in each eye. The prevalence of a neurologic pathology in our case series and the correlation between the findings of the three examined parameters (i.e., neurologic and neuro-ophthalmologic examination, duplex carotid Doppler, and brain CT with and without contrast) were assessed [Tables 1 and 2]. Almost two-thirds of them (41/68, 60%) had undergone neurologic examinations and all had neuro-ophthalmologic evaluations; the results were normal in each case.

Slightly more than one-half of the patients (36/68, 53%) had undergone duplex carotid Doppler: the results were normal or did not exceed 25% arterial narrowing in 33 of them (91.7%). Only three patients had any evidence of pathology on the duplex carotid Doppler evaluation; two (5.6%) had a narrowing of 26–51% and one (2.8%) had a narrowing of

51–75% [Table 2]. Of the 48 patients who had undergone brain CT, 42 had normal results, while some pathology was detected in 6, as follows: 2 (4.2%) had an infarct, 2 (4.2%) had a space-occupying lesion not related to optic pathways, and another 2 (4.2%) had brain atrophy [Table 2]. The two patients with abnormal CTs had lesions which were not situated in a location that might have produced a clinical entity capable of mimicking NTG, thus none of the patients with mass lesions had any characteristics suggestive of atypical NTG.

DISCUSSION

The aim of this retrospective study was to determine the benefit, if any, of a neurologic evaluation as part of the diagnostic workup for suspected NTG. None of the patients diagnosed with NTG had neuro-radiologic evidence of a mass lesion involving the anterior visual pathway. Our findings clearly showed that the prevalence of abnormalities identified by neurologic examinations, neuro-ophthalmologic evaluations, duplex carotid Doppler examinations and brain CT scans (with and without contrast) was too low to justify their implementation in diagnosing these patients in the absence of other clinical signs and symptoms. Nevertheless, part of the neuro-ophthalmologic evaluation, such as pupil reaction and color vision, might be included in a routine evaluation of optic nerve function by most ophthalmologists and could be performed without further cost. These results indicated that there is no need for neuroimaging in NTG patients who present with typical and uncomplicated NTG. These results and conclusions are quite similar to those of Girkin [16] who advocated neuroimaging only in typical NTG that progressed with severe visual loss and threat to fixation. On the other hand, in contrast to our findings, Ahmed et al. [17] suggested routine imaging in every NTG patient (notably, 6.5% of their patients were found to have intracranial tumors).

We do not think that more sensitive neuro-imaging techniques, such as magnetic resonance imaging, would have any added value. Moreover, the fact that they are also not cost-effective would preclude their use in the ordinary clinical setting. In contrast, we recommend that all patients who present with atypical NTG (i.e., younger than 50 years of age, lower levels of visual acuity, neuroretinal rim pallor, and poor correlation between the pattern or extent of visual field loss and optic disk cupping) undergo these evaluations [13].

The results of our current analyses indicate that routine neurologic workups have no diagnostic value in typical cases of NTG. It is, feasible, however, that an ophthalmologist in clinical practice would take every precaution to avoid placing the patient at risk, and consequently refer the patient for further evaluations, which likely involve exposure to radiation as well as considerable expense. At the same time, there should be awareness that most of these measures will prove to have been unnecessary.

Table 1. Duplex carotid Doppler examination results

	No. of patients	Percent
From normal to 25%	33	91.7
26–50%	2	5.6
51–75%	1	2.8
Total	36	100.0

Table 2. Computed tomography examination results

	No. of patients	Percent
Normal	42	87.5
Infarct	2	4.2
Space-occupying lesion	2	4.2
Atrophy	2	4.2
Total	48	100.0

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