Current Approaches to Low-Tension Glaucoma

This challenging condition requires individualized care.

BY CARLA J. SIEGFRIED, MD

The term *low-tension glaucoma* (LTG) refers to glaucomatous optic neuropathy in the presence of open angles, optic nerve cupping, and corresponding visual field defects when the IOP is not very high. LTG is common. Half the patients from the Baltimore Eye Study and 82% of Latino-Americans in the Los Angeles Latino Eye Study with a new diagnosis of glaucoma had an IOP of 22 mm Hg or lower.[1,2] Other populations also have a preponderance of LTG. For example, 92% of Japanese patients from a cross-sectional epidemiologic study presented with this form of glaucoma.[3]

RISK FACTORS

IOP is currently the only modifiable risk factor for the development and progression of all types of glaucoma. It is unclear why, but vascular abnormalities may play a role in LTG, as there is a higher incidence of migraine, Raynaud phenomenon, and hypotension in this patient population.[4]

Structural differences in optic nerves with larger disc areas may increase the risk of LTG. Optic disc hemorrhages (Figure) occur more frequently in LTG; if indicative of progressive damage, advanced therapy may be required. Focal nerve damage with paracentral field defects is seen more frequently in eyes with LTG as compared to primary open-angle glaucoma. Early detection of subtle focal defects of the nerve fiber layer with optical coherence tomography therefore may be helpful to guide early diagnosis and therapy.

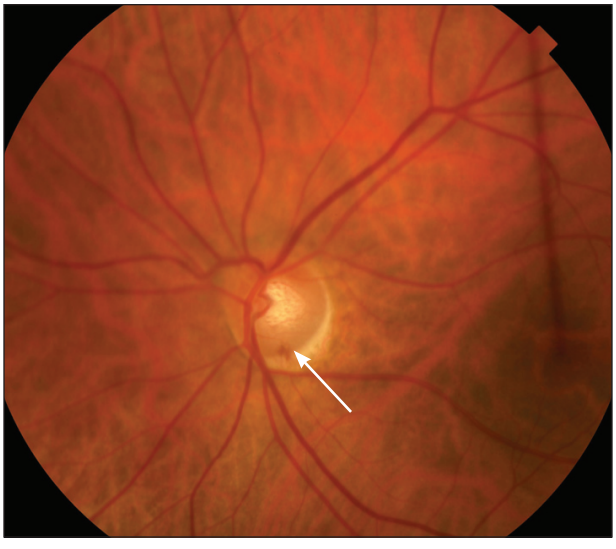

Figure. Disc hemorrhage (arrow) indicating possible progression of glaucomatous atrophy.

DIFFERENTIAL DIAGNOSIS

Careful evaluation of patients' historical data, diurnal IOP variation, optic nerve, and visual field assessment is critical to the diagnosis of glaucoma. Traumatic optic neuropathy and steroid-induced glaucoma may be diagnosed via the patient's history. Ischemic optic neuropathy (arteritic or nonarteritic) may imitate LTG in the presence of progressive optic nerve cupping. Optic nerve

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pallor and an acute onset of vision loss are also prominent findings of ischemia.

A detailed workup including neuroimaging may be indicated in patients with decreased central visual acuity (< 20/40), patients under 50 years of age, individuals with visual field defects that respect the vertical rather than horizontal midline, and those with optic nerve pallor greater than cupping.[5] Compressive lesions involving the optic nerve must be excluded in such cases.

EVIDENCE-BASED THERAPY

The Collaborative Normal Tension Glaucoma Study (CNTGS), a prospective randomized clinical trial, provided important data on the natural history and effects of IOP lowering for the treatment of LTG.[6] One eye of each eligible subject was randomized either to no treatment as a control or medical, laser, and/or surgical intervention to lower the IOP by 30% from baseline. Eyes were randomized if they met criteria for diagnosis of LTG and showed either documented progression or high-risk field defects that threatened fixation or the appearance of a new disk hemorrhage. A 30% reduction in IOP prevented visual field progression in 88% of patients with prior documented progression or field loss threatening fixation compared to 65% of the control group.

Glaucoma medications may reduce IOP to episcleral venous pressure (range, 8-12 mm Hg), so a combination of surgery and laser therapy is often indicated for select patients who show definitive progression. It is important to confirm visual field loss both at baseline and over time. Prostaglandin analogues have been shown to provide 24-hour IOP control.[7] β-blockers may contribute to systemic hypotension and decrease ocular perfusion pressure, a factor in progression in some patients with LTG. The nighttime use of β-blockers may also be avoided, as there is less aqueous humor formation and, therefore, drug efficacy during the night.[8]

In the Low-Pressure Glaucoma Treatment Study (LoGTS), the brimonidine 0.2% group was less likely to have visual field progression over a 30-month time period, but the decrease in IOP was similar to that of the timolol maleate 0.5% group. This finding suggests a possible neuroprotective mechanism not dependent on IOP.[9] Additionally, more patients dropped out of the brimonidine group due to drug intolerance. The systemic hypotensive effects of timolol may also be deleterious, as noted previously, potentially confounding the analysis of the study results.

Research in the area of neuroprotection has not yet identified agents for LTG treatment. A phase 3 clinical trial evaluating the efficacy of memantine, a noncompetitive N-methyl-D-aspartate receptor antagonist, did not show a benefit when compared with placebo. In the search for novel therapies, several other pathways are of interest.

CONCLUSION

LTG remains a challenging condition to manage over a patient's lifetime. Although 50% of patients do not show progression, those who do may suffer a significant loss of visual field and quality of life. Because IOP reduction is the only proven therapy at this time, clinicians must proceed aggressively when managing these cases. ■

Carla J. Siegfried, MD, is a professor of ophthalmology and visual sciences at Washington University School of Medicine in St. Louis. Dr. Siegfried may be reached at siegfried@vision.wustl.edu.

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