Pupil Involvement in Patients With Diabetes-Associated Oculomotor Nerve Palsy

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Objective: To derive a reliable estimate of the frequency of pupil involvement in patients with diabetes-associated oculomotor nerve palsy.

Patients and Methods: In this prospective study, standardized enrollment criteria were employed to identify 26 consecutive patients with diabetes-associated oculomotor nerve palsy who were evaluated in a referral-based, outpatient neuro-ophthalmology practice. A pupil ruler accurate to within 0.5 mm was used to measure pupil diameters using a standardized procedure. The degree of anisocoria, if present, was recorded at each office visit until the ophthalmoplegia had resolved. Descriptive statistics were used to identify the frequency and characteristics of pupil involvement.

Results: Internal ophthalmoplegia occurred in 10 (38%) of 26 patients. The size of the anisocoria was 1 mm or less in most patients. None of the patients had a fully dilated unreactive pupil.

Conclusions: Pupil involvement in patients with diabetes-associated oculomotor nerve palsy occurs more often than has been previously recognized, although the degree of anisocoria in any 1 patient is usually only 1 mm or less. Some characteristics of the internal ophthalmoplegia may help to distinguish diabetic ophthalmoplegia from injury of the oculomotor nerve caused by aneurysmal compression.


While pupil involvement associated with oculomotor nerve palsy is a sensitive predictor of aneurysmal compression, the specificity of this sign remains less clear in regard to diabetes-associated infarction. The reported frequency of pupil involvement in several series that included up to 25 patients with diabetes-associated oculomotor nerve palsy ranges from 14% to 32%. These frequencies can only be considered estimates, however, since they were derived using retrospective analyses. The absence of a standardized approach to defining diabetic ophthalmoplegia, recording pupil signs, and defining pupil involvement further contributes to the unreliability of published estimates of pupil involvement in this condition. Furthermore, it is possible that some of the patients included in older series had compressive or infiltrative lesions unrelated to diabetes. The current study was designed to overcome these limitations to derive a more reliable estimate of the frequency of pupil involvement in patients with diabetes-associated ophthalmoplegia.

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PATIENTS AND METHODS

Twenty-six patients fulfilled the enrollment criteria and were included for analysis (Table 1). Twelve (46%) of 26 patients were first evaluated within 7 days of the onset of diplopia, 18 (69%) of 26 within 14 days, and 22 (84%) of 26 within 21 days. Four additional patients were first evaluated 24, 30, 32, and 36 days after the onset of diplopia, 18 (69%) of 26 within 14 days, and 22 (84%) of 26 within 21 days. Four additional patients were first evaluated after 21 days. Twenty-four (92%) of 26 patients underwent 1 or more neuroimaging procedures, including computed tomography in 14 patients, magnetic resonance imaging in 11 patients, magnetic resonance angiography in 3 patients, and catheter angiography in 6 patients. These studies were unrevealing in all patients.

RESULTS

Some degree of anisocoria was measured in 14 (54%) of the 26 patients. None of these patients had a fully dilated, nonreactive pupil. After reviewing the course of the internal and external ophthalmoplegia of each patient, I identified 3 patterns of anisocoria that accounted for the pupillary signs in this population (Table 2).

In 4 (15%) of the 26 patients, an anisocoria measuring 0.5 mm was present at every visit, including the final one when resolution of external ophthalmoplegia was documented (Table 2). The degree of the anisocoria in these patients remained similar whether observed in room light or in dim light. The direct pupillary light reaction was normal. These characteristics are consistent with a simple anisocoria.

Seven (27%) of the 26 patients had an anisocoria that resolved completely during the course of their subse-
quent follow-up visits (Table 2 and Figure 1). The direct pupillary light reaction was variably impaired in all of these patients. The size of this anisocoria was 0.5 mm in 5 patients. One of these patients had no anisocoria when seen 1 day after the onset of diplopia at a time when her ophthalmoplegia grade was 0.5; however, when seen on day 10, she had complete external ophthalmoplegia and an anisocoria of 0.5 mm. Another of these patients had no anisocoria when first evaluated on day 5 when her ophthalmoplegia grade was 1.7; however, when she was next seen on day 12, her ophthalmoplegia grade had progressed to 2.3 and she had an anisocoria of 0.5 mm. In the remaining 3 patients who had an anisocoria of 0.5 mm, it was present at their first visits, which were 2, 18, and 30 days after the onset of diplopia when their ophthalmoplegia grades were 2.5, 4, and 4, respectively. The anisocoria was greater than 0.5 mm in 2 patients. One of these patients had an anisocoria of 1.5 mm and an ophthalmoplegia grade of 3.5 when she was first evaluated 19 days after she first noted diplopia. The other patient had an anisocoria of 2.5 mm and an ophthalmoplegia grade of 3.8 when he was first evaluated 14 days after he first noted diplopia. The course of the anisocoria in these 7 patients is consistent with internal ophthalmoplegia associated with oculomotor nerve palsy.

Three (12%) of the 26 patients had an anisocoria that decreased in size, but never resolved completely, as their external ophthalmoplegia resolved (Table 2 and Figure 1). The affected pupil demonstrated variable impairment of the direct light reaction. The size of the anisocoria when the external ophthalmoplegia resolved was 0.5 mm in all 3 patients. The direct pupillary light reaction appeared normal at that time. One of these patients was first seen on day 14 with an ophthalmoplegia grade of 4 and an anisocoria of 1.0 mm. Another patient was first seen on day 3 with an ophthalmoplegia grade of 2.4 and an anisocoria of 0.5 mm; however, when he was next evaluated on day 12, his ophthalmoplegia grade had improved slightly to 1.8, but he then had an anisocoria of 1.0 mm. The third patient had an anisocoria of 0.5 mm and an ophthalmoplegia grade of 4 when she was first seen 7 days after she noted diplopia; when she was evaluated 1 week later, her ophthalmoplegia grade was still 4 and her anisocoria had increased to 1.0 mm. The course of the anisocoria of these 3 patients is consistent with simple anisocoria superimposed on internal ophthalmoplegia associated with oculomotor nerve palsy.

In my study population, therefore, 10 (38%) of 26 patients had internal ophthalmoplegia associated with their oculomotor nerve palsy, ranging in size from 0.5 to 2.5 mm (median size, 0.8 mm) (Figure 1). The degree of anisocoria was 1 mm or less in 8 (80%) of these 10 patients. The office visit during which the maximum anisocoria was first observed occurred within 14 days of the onset of diplopia in 7 (70%) of these patients (Figure 2).

I did not identify any significant difference in the proportion of patients with pupillary involvement and those without for the abstracted clinical variables. The number of patients in each group was small, however, so that the absence of identifying an association does not necessarily imply that none existed.

The design of this study overcomes many of the methodological problems inherent in previous series report-
an autonomic neuropathy. As the neuropathy usually affects both pupils, this variable would not influence the anisocoria that develops as a result of oculomotor nerve injury in most patients. It is possible, however, that some of the patients in this series had unilateral or asymmetric pupillary autonomic neuropathy and were included in the subgroups that I classified as simple anisocoria or incompletely resolved anisocoria. Since all patients had a normal-appearing direct pupillary light reaction as their ophthalmoplegia resolved, it is unlikely that misclassification contributed substantially, if at all, to the overall results of this investigation. In fact, patients with tonic pupils were specifically excluded. In clinical practice, signs that a poorly reactive or larger pupil might be the result of long-standing diabetic neuropathy, not the result of acute oculomotor nerve injury from aneurysmal compression, include light-near dissociation and segmental paresis of the iris sphincter observed during slitlamp biomicroscopy.

After accounting for those patients with simple anisocoria, pupil involvement occurred in almost 40% of patients in my series. Methodologic differences can explain why the frequency of pupillary involvement identified in my series is higher than those estimates reported in previous series. The proportion of patients with pupillary involvement depends on how one defines the end point that distinguishes a normal pupil from an abnormal one. In this study, I prospectively measured and recorded pupil sizes to the nearest 0.5 mm in all patients. This level of scrutiny may have resulted in detection of many patients with an anisocoria of 0.5 mm. An anisocoria of such small size might have been undetected, considered insignificant, or assumed to be related to simple anisocoria by previous investigators.

In most of the patients in my series with pupillary involvement, the maximum anisocoria developed within the first 2 weeks after the onset of diplopia. Similar to a previous observation on progression of external ophthalmoplegia, the degree of anisocoria subsequently progressed in some of the patients who were first evaluated early in that 2-week period. However, since the interval between onset of symptoms and first and subsequent office visits was not uniform, the time course outlined in Figure 2 is artifactually prolonged. Had all patients been detected at a much earlier stage.

The 1- to 2-week period during which anisocoria progressed in some of the patients in this series is similar to the time frame during which the pupil may become maximally dilated in patients harboring aneurysms compressing the oculomotor nerve. A fully dilated, unreactive pupil occurs in roughly 53% to 71% of patients with aneurysmal compression of the oculomotor nerve. In contrast, the pupil was incompletely resolved anisocoria. Since all patients had minimal internal ophthalmoplegia. Additionally, most patients in my series with pupillary involvement had only minimal internal ophthalmoplegia, as evidenced by anisocoria of 1 mm or less in most of those affected. These pupil characteristics may help to distinguish diabetic (ischemic) from aneurysmal (compressive) injury of the oculomotor nerve.
American Academy of Ophthalmology Cautions Viagra Users

Physicians at the American Academy of Ophthalmology warned users about the potential side effects that may affect vision of patients who use the newly approved anti-impotence drug, Viagra.

Michael F. Marmor, MD, professor of Ophthalmology at Stanford University in Palo Alto, Calif, and spokesperson for the Academy, said that a moderate percentage of people taking Viagra have experienced problems with their vision. “FDA [Food and Drug Administration] clinical trials show that taking the medication, especially at higher doses, can cause some retinal dysfunction and affect the way we see for a number of hours.” Patients reported visual disturbances described as bluish color tinge and light sensitivity. Dr Marmor said a clinical study showed that electrical measures of retinal function dropped by 30% to 50% and lasted for at least 5 hours after taking a high dose of Viagra.

It is not known whether the drug causes any permanent changes in vision. Studies about the long-term effects of taking Viagra are needed. In the meantime, Dr Marmor urged those with retinal eye conditions such as macular degeneration or retinitis pigmentosa to use the drug with caution and to stay at the lowest dose level possible. According to the FDA, the recommended dose level for most patients is 50 mg.