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CLINICAL INVESTIGATION

Bilateral Tonic Pupils Associated with Neurosyphilis

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Background: To describe 4 patients with bilateral tonic pupils in neurosyphilis.

Cases: Four young men had pupillary abnormalities, which involved irregular shapes, large sizes, tonic reactions, and vermiform movements of both pupils with light-near dissociation. Cholinergic supersensitivity defined bilateral tonic pupils.

Observations: Neurosyphilis was diagnosed in these patients on the basis of ocular and laboratory findings.

Conclusions: Bilateral tonic pupils may be important as initial findings in neurosyphilis. We conclude that patients with bilateral tonic pupils should undergo serologic tests for syphilis. **Jpn J Ophthalmol 2003;47:368–371** © 2003 Japanese Ophthalmological Society

Key Words: Neurosyphilis, tonic pupils.

Introduction

The classic pupillary abnormality in neurosyphilis is commonly known as Argyll Robertson (AR) pupils.[1] However, the association of tonic pupils with neurosyphilis is recognized infrequently. To our knowledge, only a few papers in the literature[2–7] have reported this. We now describe four cases of bilateral tonic pupils in which laboratory and cerebrospinal fluid (CSF) studies revealed neurosyphilis.

Case Reports

Case 1

A 32-year-old man was referred for evaluation of bilateral visual disturbance and optic disc atrophy. The visual loss had started 2 years earlier and had gradually progressed. On examination, best-corrected visual acuity was 20/200 OD and 20/50 OS. The pupils measured 5.0 mm OD and 4.0 mm OS in room illumination (Figure 1A). They reacted weakly to light illumination and constricted tonically at near viewing (Figure 1B). Slit-lamp examination showed segmental constriction of both irises. The pupils constricted with 0.0625% pilocarpine (Figures 1C–F). Intraocular pressure in both eyes was 12 mm Hg. Dilated funduscopic examination demonstrated pallor of the temporal discs bilaterally without chorioretinitis. Goldmann perimetry revealed bilateral central scotomas and inferotemporal field defects. An electroretinogram was normal, and results of magnetic resonance imaging (MRI) were unremarkable. Both the serum treponema pallidum hemagglutination (TPHA) test (1:10,240 titer) and the fluorescent treponemal antibody-absorption (FTA-ABS) test were positive. The CSF showed pleocytosis, and results on the TPHA and FTA-ABS tests were positive. The patient was treated for neurosyphilis. The symptoms and findings did not improve with treatment by systemic antibiotics and corticosteroids.

Case 2

This 33-year-old man first consulted the Department of Neurology because of gait disturbance of 6-month duration. Neurologic examination revealed a broad-based gait, deep sensory disturbance, and loss of deep tendon reflexes in the ankles and knees. The patient was referred to our department for evaluation of bilateral pupillary abnormalities.

Physical examination showed 20/20 visual acuity with glasses in each eye. The right and left pupils were 6.5 and

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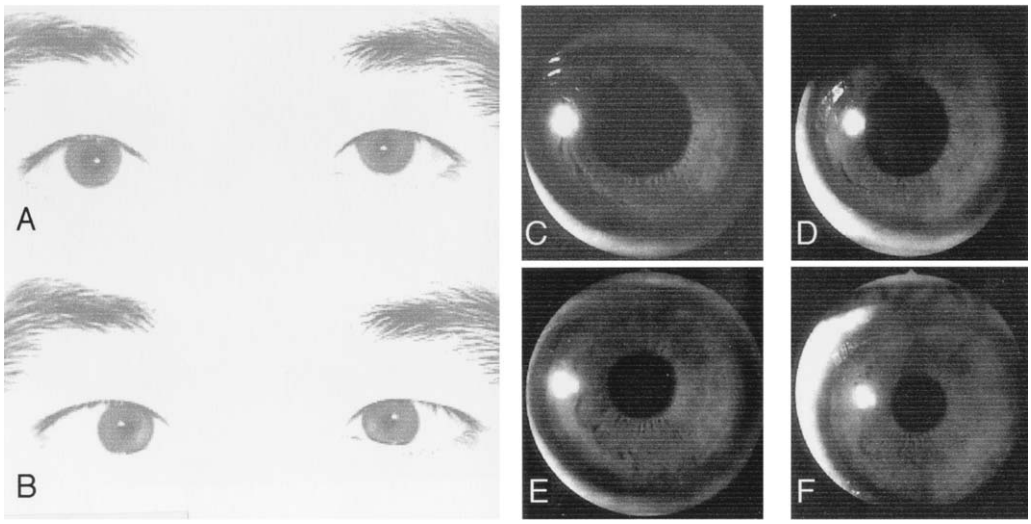

Figure 1. In Patient 1, the pupils show anisocoria in room illumination (**A**). Both pupils constrict in near viewing (**B**). After pilocarpine was administered, segmental constriction of both irises (**C** and **E**, right eye; **D** and **F**, left eye) is evident.

7.0 mm, respectively, in room illumination (Figure 2A). They were not reactive to bright light but constricted slowly to near stimuli (Figure 2B). Vermiform movements of the iris were noted on slit-lamp examination. Both pupils were sensitive to 0.0625% pilocarpine (Figures 2C–F). Measurement of the pupil diameters by infrared video-pupillography (C-2514; Hamamatsu Photonics, Hamamatsu) also showed large size (initial horizontal diameter: right, 6.3 mm; left, 6.6 mm), weak reaction to light stimulus (constriction rate: right, 0.12; left, 0.10) and supersensitivity to pilocarpine (right, 4.0 mm; left, 3.7 mm) (Figures 3A,B). Both the TPHA test (1:163,840 titer) and the FTA-ABS test were positive in serum. The CSF examination revealed pleocytosis, elevated protein, and positive TPHA and FTA-ABS. Neurosyphilis was diagnosed. After treatment with high-dose oral penicillin, the tonic pupils were unchanged, but the patient's gait disturbance improved slightly.

Case 3

A 37-year-old man had had visual disturbance for 4 months. The patient was referred to us for evaluation of visual impairment. Examination revealed best-corrected

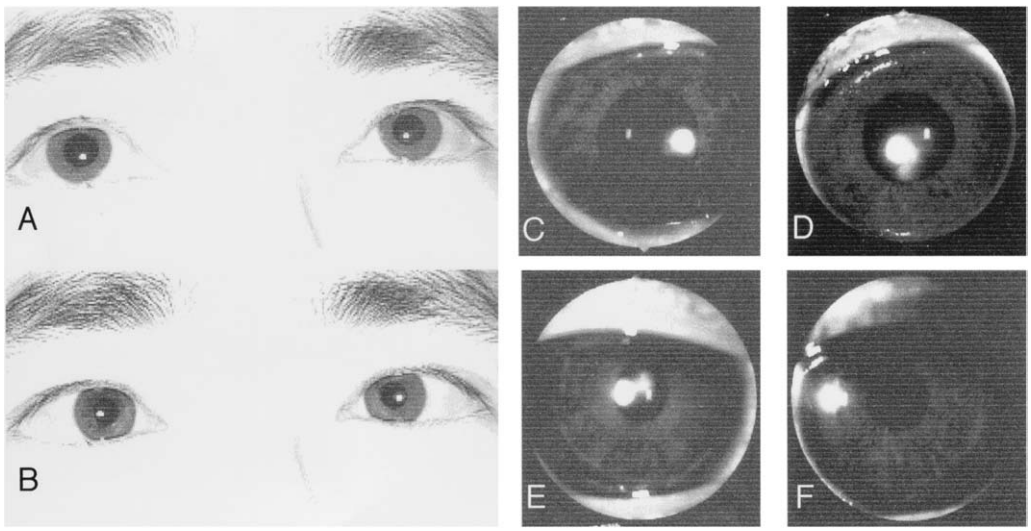

Figure 2. In Patient 2, the pupils show anisocoria and mydriasis in room illumination (**A**). Both pupils constrict to near stimuli (**B**). After pilocarpine administration, both pupils (**C** and **E**, right eye; **D** and **F**, left eye) are constricted.

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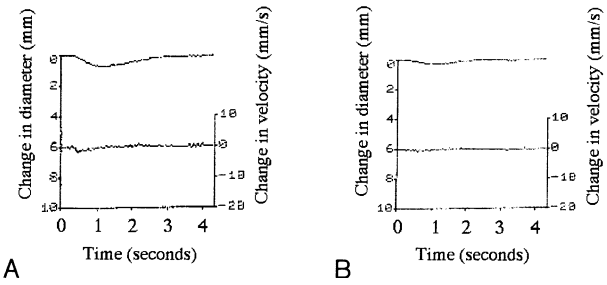

Figure 3. The data from infrared video-pupillogram of right pupil in Patient 2 before (**A**) and after (**B**) pilocarpine administration. Upper line indicates change in maximal horizontal diameter with light reflex. Lower line indicates change in velocity with light reflex. Initial diameter is set to zero in left ordinate. Right ordinate indicates change in velocity with light reflex. The pupil reacted weakly to light and constricted markedly after administration of 0.0625% pilocarpine.

visual acuity of 20/250 OD and 20/600 OS. The right and left pupils were 4.0 and 3.5 mm, respectively, in room illumination. They were nonreactive to bright light, but constricted slowly on accommodation. Vermiform movements of the iris were noted on slit-lamp examination. Both pupils were sensitive to 0.0625% pilocarpine. Funduscopic examination demonstrated pale discs bilaterally. Both the TPHA test (1:20,480 titer) and the FTA-ABS test were positive in serum. The CSF examination revealed positive results on the TPHA and FTA-ABS tests. A diagnosis of neurosyphilis was made on the basis of these results. After treatment with high-dose oral penicillin, the visual impairment remained unchanged.

Case 4

A 42-year-old man was referred to us because of acute onset of diplopia on left gaze. Abduction of the left eye was limited. Corrected visual acuity was 20/20 in each eye. The right and left pupils were 6.0 and 6.5 mm, respectively, in room illumination. They were not reactive to bright light but constricted slowly on near viewing. Vermiform movements of the iris were found on slit-lamp examination. Both pupils were sensitive to 0.125% pilocarpine. Goldmann perimetry showed no abnormal findings. Both the TPHA (1:20,480 titer) and FTA-ABS tests were positive in serum and in CSF. Neurosyphilis was diagnosed. After treatment with high-dose oral penicillin, the pupils remained unchanged, but the ocular motility improved slightly.

Discussion

AR pupils with miosis and light-near dissociation are a typical pupillary abnormality in neurosyphilis.[1] However, some previous reports have noted that not all syphilitic pupils are typical AR pupils.[8,9] Lowenfeld[1] has suggested that 75% of patients do not show AR pupils. Moreover, Meritt et al[8] have reported that 64% of patients with tabetic neurosyphilis do not have AR pupils, and Okada[9] has reported that only 12% of patients with neurosyphilis have AR pupils. These reports indicate that the AR pupils in neurosyphilis are specific but rare.

Tonic pupils may resemble AR pupils in several ways: (1) light-near dissociation, (2) irregular pupillary shape, and (3) unequal pupillary size. Tonic pupils may be differentiated from AR pupils on the basis of the sex ratio, the mean age, pupillary size, laterality, tonic reaction, vermiform movements, and cholinergic supersensitivity. In our cases, on the basis of tonic reaction, vermiform movements, and cholinergic supersensitivity, the pupils were diagnosed as tonic pupils, not AR pupils. Tonic pupils tend to become smaller and bilateral with time in the chronic stage,[3] and mimic AR pupils. Therefore, in some previous reports, tonic pupils in neurosyphilis might have been confused with AR pupils.

Fletcher and Sharpe[2] have reported five cases of bilateral tonic pupils in neurosyphilis. Our cases are similar to these cases and differ from cases with idiopathic tonic pupil in several ways. All our patients were men, and the male:female ratio in Fletcher's report was 1.5:1, as opposed to a male:female ratio of 1:2.2 to 1:2.6 in cases of idiopathic tonic pupils.[10] Our cases and these of Fletcher et al had bilateral tonic pupils, whereas 80% of idiopathic tonic pupils are unilateral. The mean age of detection of tonic pupils was 36 years in our cases and 57 years in those of Fletcher et al. The difference may be associated with a dramatic rise in incidence of syphilis among heterosexual men and women and drug abuse among the young in recent years. Thompson[3] has reported that the mean age of onset of Adie's pupils is approximately 32 years. Therefore, syphilitic tonic pupils may be difficult to differentiate from idiopathic tonic pupils on the basis of mean age.

Although the lesions that cause the tonic pupils are certainly located in the ciliary ganglion or postganglionic parasympathetic pathway, the etiology of tonic pupils remains unknown.[11] We speculate that tonic pupils in syphilis might have provided evidence that ciliary ganglions or postganglionic parasympathetic neurons were affected by inflammation and ischemia.

We observed optic atrophy in 2 of our patients, as did Fletcher et al in 1 patient. Although Bruetsh[12] has reported that optic atrophy is a common finding in patients with tabes dorsalis, our patients and the patient of Fletcher et al had no tabetic symptoms or other neurologic disorders. Therefore, we infer that the optic atrophy might have been a secondary change due to syphilitic optic

neuritis or meningovascular syphilis. Characteristic findings of syphilitic optic neuritis include retinal lesions with disc edema, splinter hemorrhage, and vitreous opacity. Visual examination typically shows an enlarged blind spot and paracentral scotoma. Some patients with meningovascular syphilis have slowly progressive visual loss associated with evidence of optic nerve dysfunction.[12] Additionally, optic nerve disorders due to meningovascular syphilis are usually bilateral, and the optic discs gradually become atrophic owing to progressive ischemia.[12] Although we do not rule out the possibility of syphilitic optic neuritis in our cases, the optic atrophy might have been caused by meningovascular syphilis. Finally, although the visual disturbances in our cases did not improve, treatment may have prevented the development of hemiparesis, aphasia, and other focal neurologic deficits.

In conclusion, bilateral tonic pupils are rare but may be important as the initial sign in neurosyphilis. Although most patients with tonic pupils do not have neurosyphilis, we suggest that patients with bilateral tonic pupils undergo serologic tests for syphilis. Early diagnosis and treatment may prevent further progression of neurosyphilis.

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