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Reversible Horner’s Syndrome and Lyme Disease

Tracy A. Glauser, M.D., Patrick J. Brennan, M.D., and Steven L. Galetta, M.D.

Neurologic manifestations of Lyme disease are common, often debilitating, and potentially treatable. We document a case of *Borrelia* infection of the nervous system manifesting as a reversible Horner’s syndrome. The search for Lyme disease should be part of the evaluation of an isolated central or preganglionic Horner’s syndrome or any unexplained pupillary abnormality.

**Key Words:** Lyme disease—Horner’s syndrome—Pupillary abnormality.

Lyme disease is a multisystem spirochetal infection caused by *Borrelia burgdorferi* and transmitted by Ixodid ticks (1-3). After infection the characteristic rash, erythema chronicum migrans, and non-specific constitutional symptoms may ensue. Untreated primary infection may result in various neurologic, cardiac, or joint abnormalities (1-3). The most common neurologic presentations are aseptic meningitis, radiculoneuritis, and cranial neuritis (2-5). This case represents the first report of Lyme disease associated with a reversible Horner’s syndrome as its sole neurologic manifestation.

**CASE REPORT**

The patient was a 30-year-old, previously healthy, right-handed white man who spent most of his leisure time during the month before presentation hunting and skinning deer in southeast Pennsylvania. He felt well until 4 days before evaluation when he discovered a large tick on his neck that he burned with a cigarette and removed with tweezers. The following day he developed a headache, low-grade fever, chills, myalgias, malaise, and stiff neck. Forty-eight hours later, the patient found an erythematous circular “target-shaped rash” on his left calf. That morning he had an episode of lightheadedness while urinating and slumped against the wall. This prompted him to visit a local emergency room, where he was diagnosed with Lyme disease and tetracycline therapy was started at 500 mg orally four times a day. The patient felt better by the next day but noticed that his pupils were unequal and his left lid was drooping. He came to the Hospital of the University of Pennsylvania for further evaluation and was admitted.

On physical examination, the patient appeared
well developed and well nourished. His temperature was 98.3°F and the remainder of his vital signs were normal. General examination revealed a 16-cm erythematous "target" lesion on his left calf with partial central clearing. It was not vesicular, warm, tender, or indurated. There were no other cutaneous lesions. His neck was slightly stiff and some pain was elicited on full flexion. Results of the cardiopulmonary and abdominal examinations were completely normal.

Neurologic examination revealed the patient to be awake, alert, and oriented to time, place, and person. His mental status was completely intact except for being anxious. Visual acuity was 20/20 bilaterally and his visual fields were full to confrontation. On funduscopic examination, his disks were sharp and flat. There was a 2-mm left ptosis (Fig. 1). In ambient light, the right pupil was 5 mm and reduced briskly to 2 mm on light stimulation. The left pupil size was 3½ mm and, with light stimulation, reduced briskly to 2 mm. When the patient was placed in a dark room, the right pupil dilated to 6½ mm, while the left pupil exhibited a dilatation lag and reached only 4 mm. No afferent pupillary defect was seen. Extraocular motility was full. Facial sensation and strength were symmetric and normal. No abnormalities in hearing were detectable. His palate elevated symmetrically and the gag response was strong. Sternocleidomastoid strength was normal and the patient protruded his tongue in the midline. Muscle bulk, tone, and strength were normal in all extremities. The modalities of light touch, pinprick, temperature, vibration, and proprioception were all intact. Deep tendon reflexes were normal and his plantar responses were downgoing. The patient had a normal gait and there was no dysmetria.

Ten percent cocaine eye solution instilled in both eyes produced a 1½-mm increase in the baseline anisocoria. This confirmed the presence of a left Horner’s syndrome. Twenty-four hours later, instillation of 1% hydroxyamphetamine (Paredrine) led to both pupils enlarging to 8½ mm with improvement of the left ptosis. Old photographs were reviewed and did not reveal a prior Horner’s syndrome.

Dermatologic consultation advised that the oval erythematous target-like lesion on the patient’s left calf was consistent with erythema chronicum migrans. Therapy was initiated with Ceftriaxone 1 g intravenously every 12 h for 10 days.

Laboratory results on admission included normal complete blood count with differential, serum electrolytes, prothrombin time, and partial thromboplastin time. Rapid plasma reagin (RPR) titer was negative. An erythrocyte sedimentation rate was elevated to 27 mm/h. The patient’s alkaline phosphatase, γ-glutamyltransferase, alanine transaminase, and aspartate transaminase were all mildly elevated. Chest x-ray, electrocardiogram, and urinalysis results were all normal. Magnetic resonance imaging scans of the patient’s head and cervical spine were normal. Cerebrospinal fluid examination showed 1 WBC/mm³ (all lymphocytes), 3 RBC/mm³, a glucose level of 72 mg/dl, and a protein level of 28 mg/dl. Lyme IgG and IgM titers from the patient’s local hospital were within normal limits. Lyme enzyme-linked immunosorbent assay (ELISA) titer done on admission was 0.74 (normal up to 0.90) and Lyme IgM titer was <1:20.

Two weeks after initial presentation, the patient’s Lyme ELISA titer was 2.60 and Lyme IgM titer was 1:64, confirming the diagnosis. Titers from a different laboratory showed a Lyme ELISA of 1.91. A hepatitis screen gave a negative result, and the liver function tests were normalizing. One month after presentation (2 weeks after therapy), reevaluation showed a minimal left ptosis and almost complete resolution of the anisocoria (Fig. 2). There were no new neurologic complaints and the neurologic examination was otherwise unchanged.

**DISCUSSION**

Although Lyme disease was not recognized in the United States until 1975, its symptoms were
HORNER’S SYNDROME AND LYME DISEASE

described in Europe as early as 1909 (2). At that
time, erythema chronicum migrans was recog-
nized to be a result of tick-mediated infection. Be-
ing in 1922, neurologic sequelae of tick-borne
infections were detailed (2,3). The European syn-
drome, consisting of dermatologic and neurologic
symptoms after an Ixodes ricinus tick bite, was
known by various names, including Garin-
Bujadoux syndrome, Bannwarth syndrome, and
tick-borne meningoradiculoneuritis (2–4). The
American version of this illness, first called Lyme
arthritis, was recognized after identification of a
group of children near Lyme, Connecticut, who
had been misdiagnosed with juvenile rheumatoid
arthritis (1–3). During the following years, it was
realized that the illness involved not only the joints
and skin but also the central nervous system and
heart, and was renamed Lyme disease (2,3).

A number of studies have chronicled the scope
and severity of the neurologic manifestations of
Lyme disease (2–5). The neurologic signs usually
present several weeks after the start of the illness,
but may be the presenting manifestation of the dis-
order. The most common neurologic symptoms
are meningoencephalitis, radiculoneuritis, and
cranial neuritis (2–5). The meningoencephalitides
may be short-term or chronic, and the cerebrospi-
nal fluid usually has a pleocytosis or lymphocyto-
sis, along with an elevated protein level (2–5).
Basal meningeovasculitis and occlusion of the basi-
lar artery has been reported in association with
Borrelia burgdorferi infection (6). Radiculopathies
can be motor or sensory, unilateral, or bilateral.
Brachial plexitis and mononeuritis multiplex have
also been reported (3–5).

The facial nerve is the most commonly involved
cranial nerve (2–5) and can be involved either uni-
laterally or bilaterally. Lesions of every cranial
nerve from the oculomotor to the spinal accessory
nerve have been documented in patients with
Lyme disease (4,7). The optic nerves have not been
spared by Borrelia. Papilledema has been reported
(8). Another case initially thought to show papill-
edema (9) probably was “optic neuritis with good
vision or optic perineuritis” (10) because the cere-
brospinal fluid opening pressure on presentation
was normal and visual fields revealed “bilateral
cocentral scotomas” (10). In addition, patients
have been reported to have had Argyll Robertson
pupils (8), iritis, and vitritis (10).

This patient presented with a history of expo-
sure to ticks, and the rash of erythema chronicum
migrans. The clinical diagnosis of Lyme disease
was serologically confirmed. The patient’s neuro-
logic examination was completely normal except
for a left Horner’s syndrome that was pharma-
cologically proved using 10% cocaine eye drops. One
percent hydroxyamphetamine was used to localize
the lesion within the three-neuron oculosympa-
thetic pathway. Because both pupils dilated to 8½
mm after Paredrine instillation the lesion had to be
either in the first- or second-order neuron.

A central Horner’s syndrome occurs when the
first neuron in the oculosympathetic pathway is
damaged. The majority of lesions to this neuron
are due to brainstem or cerebral vascular insults
(11,12). However, intracranial and intraspinal tu-
mors, syringomyelia, multiple sclerosis, and
trauma represent other common important etiolo-
gies of a central Horner’s syndrome (11,12). A pre-
ganglionic Horner’s syndrome occurs when the
second neuron in the oculosympathetic pathway is
damaged. Lesions to this neuron are usually the
result of tumor involvement or trauma. The most
common tumor involving this second-order neu-
ron is bronchogenic carcinoma (Pancoast’s tumor).
However, breast cancer, sarcomas, lymphoreticu-
lar disease, and vertebral column and meningal
tumors have been documented to cause pregangli-
onic Horner’s syndrome. Less common causes of
preganglionic Horner’s syndromes include the pa-
chymeningitis of syphilis, ruptured intervertebral
disks, and thoracic aneurysms (11,12).

In this patient there was no evidence of a vas-
cular insult, malignancy, syringomyelia, or multi-
ple sclerosis because both head and cervical spine
magnetic resonance imaging scans and chest x-ray
films were normal. There had been no history of
trauma or recent neck or thoracic surgery. Our pa-
tient’s Horner’s syndrome appeared concurrently
with the Borrelia infection and resolved with cef-
triaxone therapy.

The natural history of Lyme disease may vary
considerably and often presents a difficult diag-
nostic challenge. It has become increasingly evi-
dent that the three stages of Lyme disease may
overlap, allowing certain features to appear out of
sequence or to occur in isolation (13). Given the
early onset of this patient’s Horner’s syndrome
and its rapid response to therapy, we believe the
most likely pathophysiologic mechanism was di-
rect invasion of the spirochete into the sympathetic
pathway. Similar to the facial nerve palsy associ-
ated with this disorder (14), a Horner’s syndrome
may occur in the absence of a cerebrospinal fluid
pleocytosis.

In patients with new onset isolated central or
preganglionic Horner’s syndrome, Lyme disease
should be carefully considered. Unlike most cases
of Horner’s syndrome, it can be treated and re-

1 Clin Neuroophthalmol, Vol. 9, No. 4, 1989
versed. The neurologic presentations of Lyme disease are so diverse that serologic tests for Lyme infection are probably essential in the diagnostic evaluation of patients with unexplained pupillary abnormalities.

REFERENCES

Herpes Zoster Ophthalmicus, Contralateral Hemiplegia, and Recurrent Ocular Toxoplasmosis in a Patient with Acquired Immune Deficiency Syndrome–Related Complex

Sasikala Pillai, M.D., Muneera A. Mahmood, M.D., and Suresh R. Limaye, M.D.

A 42-year-old man presented with herpes zoster ophthalmicus on the right side. He was found to have acquired immune deficiency syndrome–related complex. Two weeks later he developed toxoplasmic retinochoroiditis in the left eye. He also presented later with left hemiplegia, which was probably caused by herpes zoster arteritis. Nine months after the retinal lesion resolved he developed another area of toxoplasmic retinochoroiditis adjacent to the first lesion. Herpes zoster may be the first presentation of acquired immune deficiency syndrome–related complex in a young healthy individual. Ophthalmologists are encountering patients with acquired immune deficiency syndrome who may have multiple organisms as the cause for their ocular infections and this might pose a treatment dilemma. The combination of herpes zoster ophthalmicus and ocular toxoplasmosis in this patient makes this case unusual.

Key Words: Acquired immune deficiency syndrome–Herpes zoster ophthalmicus–Contralateral hemiplegia–Ocular toxoplasmosis.

Acquired immune deficiency syndrome (AIDS) is an infection caused by human T-cell lymphotropic virus (HTLV) and is characterized by a severe disturbance of cell-mediated immunity that leads to opportunistic infections in previously healthy individuals. The occurrence of systemic toxoplasmosis in AIDS is common, but only nine reports of ocular toxoplasmosis in AIDS have been published. We are presenting a patient diagnosed as having herpes zoster ophthalmicus and AIDS–related complex (ARC) who later developed recurrent ocular toxoplasmosis in the other eye.

CASE REPORT

On September 9, 1985, a 42-year-old man presented with a 1-week history of painful vesicles on the right side of face and scalp. He gave a history of an upper respiratory tract infection with cough and a “rundown feeling” for 2 weeks. He had chicken pox during childhood. He admitted to occasional marijuana use and gave a history of one episode of homosexual activity at the age of 15 years, but also had many female sexual contacts. On initial examination the best corrected visual acuity was OD 20/20, OS 20/20. There were small vesicular lesions in the distribution of the ophthalmic division of the fifth cranial nerve on the right side. There were conjunctival hyperemia and old keratitic precipitates on the same side. A clinical diagnosis of right herpes zoster ophthalmicus was made. Topical gentamicin drops were prescribed. He was also seen by the dermatologist who prescribed 60 mg prednisone daily for 5 days, reduced...
thereafter by 5 mg daily. Three days later he presented with acute granulomatous anterior uveitis in the right eye and was prescribed 2% homatropine and 1% Pred Forte eyedrops four times daily. Two weeks after the initial presentation with herpes zoster ophthalmicus he complained of malaise and developed swelling of both knees. His visual acuity was OD 20/20 and OS 20/80. He now had granulomatous anterior uveitis in the left eye. There were 2+ cells in the vitreous with a peripheral necrotizing retinal lesion in the superior temporal quadrant of the retina and a small choroidal scar nasally; these findings were consistent with a clinical diagnosis of toxoplasmic retinochoroiditis. Oral prednisone was discontinued. Physical examination at this time revealed axillary and inguinal lymphadenopathy. Laboratory test results showed a corrected sedimentation rate of 27 (normal 0–10); white blood cell count (WBC) was 4.1 x 10³. Fluorescent treponemal antibody-absorption reactive and microhemagglutination assay for antibodies to T. pallidum (MHA-TP) were reactive; rapid plasma reagin nonreactive, fluorescent anti-nuclear antibody, and rheumatoid factor tests were negative. The patient had been treated for syphilis many years ago. Serum toxoplasmosis titer (IgG immunofluorescent antibody) was 1:3,192. The patient's serum was positive for HTLV III antibody by enzyme-linked immunosorbent assay and he had an abnormal helper-to-suppressor T-lymphocyte subset ratio. He was anergic to cutaneous mumps and purified protein derivative (PPD) injections. Radiologic examination of the chest showed changes that suggested emphysema in both lungs. He was treated with 150 mg Daraprim oral loading dose followed by 25 mg twice daily, 3 g Sulfadiazine loading dose followed by 1 g four times daily and 3 mg folinic acid once a week for 6 weeks. Topical use of 1% Pred Forte and 2% Homatropine was continued in OD and started in OS. One week after commencing treatment the retinal lesion became flatter and pigmentation was noted at the edge of the lesion. Two months after his initial presentation he developed nerve fiber layer infarcts in both eyes (Fig. 1). On November 15, 1985 he presented to the emergency room with left sided facial weakness and left hemiplegia. He was admitted to the hospital. A
cerebrospinal fluid tap showed protein 43 mg/dl, glucose 47 mg/dl, WBC 9/mm³, RBC 5/mm³, differential 25% polymorphonuclear cells and 75% lymphocytes. Gram stain, India ink preparation, venereal disease reference test (VDRL) and routine cultures from the cerebrospinal fluid were negative. Because VDRL was negative in cerebrospinal fluid, the neurologist felt that the patient did not require intravenous aqueous penicillin. Computed axial tomography (CAT) scan of the brain was normal. T-lymphocyte helper-to-suppressor ratio (T4/T8) was 0.43 (normal 1.2-8.8). Serum toxoplasmosis titer (IgG immunofluorescent antibody) was 1:16,384. Blood cultures were negative but urine cultures were positive for candida. The patient refused to have a carotid angiogram at this time. His clinical condition improved, and he was discharged from the hospital after 13 days. On February 27, 1986 he had 20/25 vision OD. The toxoplasmic retinochoroiditis had resolved. Serum toxoplasmosis titer was negative. He still had some residual motor and sensory deficit on the left side. A carotid angiogram done 6 months after the onset of hemiplegia showed no abnormality.

On October 1, 1986 a fluffy white 1½ disc diameter retinal lesion was noted adjacent to the healed toxoplasma lesion in the superotemporal quadrant of the left eye. The vitreous reaction was moderate. Serum toxoplasmosis titer was 1:16. Since the lesion looked clinically like toxoplasmic it was again treated with dapsone, sulfonamides, and folinic acid. The repeat T4/T8 ratio was 0.14 (normal 1.2-3.8). After treatment the vitreous appeared less hazy and the retinal lesion had regressed, showing pigmentation. The ocular findings remained the same until the time of his death in March, 1987. He died from complications arising from Pneumocystis carinii pneumonia and atypical mycobacterial pulmonary infection.

COMMENT

AIDS patients are susceptible to a variety of opportunistic infections, which include Pneumocystis carinii pneumonia, candidiasis, cytomegalovirus infections, herpes simplex infections, hepatitis B virus infections, toxoplasmosis, cryptococcosis, and atypical mycobacterial infections (1). Cone and Schiffman (2) suggested that the development of herpes zoster ophthalmicus in a previously healthy individual indicated an immunologic aberration that could ultimately evolve into AIDS. Two of their four patients with herpes zoster had reduction in T-helper cells and a reversal of T-cell helper/suppressor ratio. Sandor et al. (3) evaluated 25 consecutive cases of herpes zoster ophthalmicus and identified a subgroup of persons distinguishable by the presence of AIDS risk factors in association with a diminished helper T-cell population and polyclonal elevation in gamma globulin. Cole et al. (4) described four cases of herpes zoster ophthalmicus in homosexual men; two of them had AIDS and two had ARC. In a prospective investigation of 54 consecutive cases of herpes zoster ophthalmicus, Sandor et al. (5) found that over a 2-year period, 21% of the AIDS-risk subgroup developed AIDS. He suggested that systemic corticosteroids for treatment of herpes zoster ophthalmicus should be avoided in individuals with risk factors associated with AIDS. None of their patients showed any of the ocular manifestations associated with AIDS during the acute phase of herpes zoster ophthalmicus. During the 2½-year followup one patient had necrotizing retinitis and died of central nervous system toxoplamosis.

Manifestations of herpes zoster encephalitis may appear between 1 week before and 8 weeks after the onset of the cutaneous eruption. Most cases occur within 2 weeks after the rash is seen (6). Laboratory findings in the cerebrospinal fluid include an increase in the leukocyte count, mostly mononuclear cells, and moderate elevations of protein. Mackenzie and colleagues (7) suggested that the virus spreads along the intracranial branches of the fifth nerve to the intracranial portions of the internal carotid artery, and to the first 2 cm of the middle cerebral artery, the first 3 cm of the anterior cerebral artery, and to the large arteries at the base of the brain. Hilt et al. (8), in his review of patients with herpes zoster ophthalmicus and contralateral hemiparesis, found that although the neurological manifestations were usually monophasic, some patients had recurrent episodes of angiitis in the distribution of the middle cerebral artery. Segmental narrowing of the proximal middle cerebral, anterior cerebral, and distal internal carotid artery have been documented by Walker et al. (9), Mackenzie et al. (7), and Bourdette et al. (10). CAT scans have shown lesions consistent with infarction in the distribution of the middle cerebral artery (8,11). Postmortem examination has revealed fulminant vasculitis with viral particles in vascular smooth muscle cells, as shown by Linnemann and Alvira (12) and Doyle et al. (13). The occurrence of systemic toxoplasmosis in patients with AIDS is quite common. However, there have been only nine reports of ocular toxoplasmosis in patients with AIDS (Table 1). Our patient is unusual in that he presented with herpes zoster ophthalmicus and was diagnosed to have...
ARC. He received oral prednisone (615 mg total dose) to prevent postherpetic neuralgia. While he was taking oral steroids he developed toxoplasmic retinochoroiditis in the other eye. Nozik and O’Connor (21) attempted to reactivate healed, experimentally induced toxoplasmic retinochoroiditis in the rabbit with systemically administered corticosteroids, and were unsuccessful. Kaufman (22) suggested that acute disseminated infection (as in congenital toxoplasmosis) in the absence of effective immunity is made lethal by corticosteroids, but that the ocular disease of chronic toxoplasmosis does not exacerbate or become lethal with steroid therapy. Our patient developed hemiplegia, which was presumed to be due to viral cranial vasculitis. Since a carotid angiogram was not done during the acute phase it was not possible to confirm the diagnosis. After that time he developed nerve fiber layer infarcts in both eyes and reactivation of toxoplasmic retinochoroiditis in the left eye.

The most recent serum toxoplasmosis titer was only 1:16, which may indicate further worsening of his immune deficiency. Although his T-lymphocyte helper-to-suppressor ratio decreased further, he remained free from opportunistic infections associated with AIDS until the time of his death in March 1987. The possibility of AIDS or ARC should be considered in young patients who present with herpes zoster ophthalmicus. Ocular toxoplasmosis is being more frequently reported in patients with ARC or AIDS.

### TABLE 1. Findings in patients with AIDS and ocular toxoplasmosis

<table>
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<th>Associated conditions</th>
<th>CNS toxoplasmosis</th>
<th>Ocular toxoplasmosis</th>
<th>Method of diagnosis</th>
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<tr>
<td>Sandor et al. (5)</td>
<td>AIDS</td>
<td>Encephalitis</td>
<td>Necrotizing retinitis</td>
<td>Unknown</td>
</tr>
<tr>
<td>Parke and Font (14)</td>
<td>AIDS, cryptococcal meningitis</td>
<td>Negative</td>
<td>Unilateral acute retinal necrosis; no scars</td>
<td>After enucleation</td>
</tr>
<tr>
<td>Schuman and Friedman (15)</td>
<td>Case no. 1 AIDS, Pneumocytis carinii pneumonia</td>
<td>Brain abscess</td>
<td>Unilateral retinochoroiditis; no scars</td>
<td>After enucleation</td>
</tr>
<tr>
<td>Alonso et al. (17)</td>
<td>AIDS, Cytomegalovirus</td>
<td>Lesion in right basal ganglia</td>
<td>Retinochoroiditis initially</td>
<td>Clinical features</td>
</tr>
<tr>
<td>Weiss et al. (18)</td>
<td>AIDS, Candida</td>
<td>Negative</td>
<td>Retinochoroiditis initially, no scars</td>
<td>Vitreous culture</td>
</tr>
<tr>
<td>Snider et al. (19)</td>
<td>AIDS, candida</td>
<td>Lesion in right basal ganglia</td>
<td>Retinochoroiditis initially</td>
<td>After enucleation</td>
</tr>
<tr>
<td>Friedman (20)</td>
<td>AIDS, Pneumocystis carinii pneumonia</td>
<td>Frontal abscess initially</td>
<td>Retinochoroiditis initially, no scars</td>
<td>Vitreous culture</td>
</tr>
</tbody>
</table>

### REFERENCES

15. Schuman JS, Friedman AH. Retinal manifestations of the AIDS: cytomegalovirus, Candida albicans, Cryptococcus, Tox...


Editorial Comment

Diagnosing Neurosyphilis
The Value of the Cerebrospinal Fluid VDRL or Lack Thereof

In their description of a patient with AIDS, herpes zoster ophthalmicus and recurrent ocular toxoplasmosis, Pillai and colleagues (1) state that their neurological consultant did not feel that the patient required intravenous penicillin for neurosyphilis because his cerebrospinal fluid (CSF) venereal disease research laboratory test (VDRL) was negative. This belief regarding the CSF VDRL, though widely held, is mistaken. The VDRL is a nontreponemal reaginic test in which serum or CSF is tested for its ability to flocculate a suspension of cardiolipin–cholesterol–lecithin. The immunoglobulins responsible for a positive response are directed against a lipoidal antigen that results from an interaction of Treponema pallidum with host tissues and/or T. pallidum itself. In the serum, a positive VDRL is neither sensitive nor specific for syphilis and requires confirmation with specific treponemal tests, such as the fluorescent treponemal antibody-absorption test (FTA-abs), microhemagglutination assay for antibodies to T. pallidum hemagglutination assay (MHA-TP), or the T. pallidum immobilization (TPI) test. The serum VDRL is positive in 72% of patients with primary syphilis, in nearly 100% of patients with secondary syphilis, in 73% of patients with latent syphilis, and in 77% of patients with tertiary syphilis (2). Therefore, one-quarter of patients with neurosyphilis have a negative serum VDRL. In the presence of concomitant HIV infection, the likelihood of a false-negative serum VDRL may be even higher. For instance, Hicks and colleagues (3) reported a HIV-seropositive patient with secondary syphilis and negative serological studies. The diagnosis of syphilis was established by dark-field examination of the patients skin biopsy.

The nontreponemal reaginic test widely used before the development of the VDRL slide test was the Wasserman test. Merritt et al. reported that the incidence of a positive CSF Wasserman test in the face of neurosyphilis varied from 81% in meningeovascular syphilis to 100% in tabes dorsalis and spinal pachymeningitis (4). However, tabes dorsalis has been clinically diagnosed in patients with a nonreactive CSF Wasserman test (5). Additionally, pathologically confirmed neurosyphilis has been reported in a patient with a nonreactive CSF VDRL test (6). In a study by the Centers for Disease Control, the CSF VDRL was positive in 90% of patients with symptomatic neurosyphilis, but only in 10% of patients with asymptomatic neurosyphilis (7). However, the insensitivity of the VDRL in the latter group may have reflected their definition of asymptomatic neurosyphilis. Recently, Lukehart and colleagues cultured CSF from patients with untreated syphilis in rabbit testicles (8). This test is the "gold standard" for establishing the presence of T. pallidum infection in the central nervous system; however, it is impractical to perform and available in only a handful of medical centers. Treponemes were demonstrated in the CSF of 12 (30%) of 40 patients with primary and secondary syphilis (8). The CSF VDRL was positive in only 4 (33%) of the 12 patients from whom CSF treponemes were isolated (8). Therefore, measures other than a positive CSF VDRL must be relied on to establish a diagnosis of neurosyphilis.

Unfortunately, no consensus exists regarding the diagnostic criteria for neurosyphilis. At one end of the spectrum, a diagnosis of neurosyphilis has been recommended in patients with serological evidence of syphilis and one or more of the following abnormalities in their CSF: a pleocytosis, an elevated protein level, a decreased glucose concentration, or a positive VDRL (9). In the presence of concomitant human immunodeficiency virus infection, however, a CSF pleocytosis and elevated CSF protein are frequently observed (10). Furthermore, other useful clues for neurosyphilis, such as elevated CSF immunoglobulins or the presence of...
CSF oligoclonal bands, are often detected (10), which seriously detracts from their diagnostic utility. At the other extreme, a reactive CSF with increased cell count and protein level and a positive CSF VDRL have been the diagnostic requirements for neurosyphilis proposed by others (11). Clearly, the appropriate answer lies somewhere between these two extremes. A reliable CSF test that exhibits both a high degree of sensitivity and specificity for neurosyphilis would be ideal. The currently available treponemal tests are hardly ideal for this purpose (12), and the physician must refrain from dogma in making this diagnosis. Perhaps the development of newer generation tests, such as polymerase chain reaction or monoclonal antibodies for syphilis, may solve our current dilemma.

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REFERENCES


Schilder’s Myelinoclastic Diffuse Sclerosis

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We report here a case of Schilder’s myelinoclastic diffuse sclerosis in a 14-year-old girl with sudden bilateral visual loss. Computed tomographic scan showed two large symmetrical lesions in the occipital lobes and a smaller hypodense area in the frontal lobe. Cerebrospinal fluid examination revealed increased immunoglobulin G fraction with the presence of oligoclonal bands. Ultrastructural study of a biopsy specimen disclosed a demyelinating disorder with no cytoplasmic inclusions. Steroid treatment was followed by a dramatic response, with almost complete visual recovery and shrinkage of the lesions.

Key Words: Schilder’s myelinoclastic sclerosis—Demyelinating diseases—Adrenoleukodystrophy.

Few well-documented cases of Schilder’s myelinoclastic diffuse sclerosis 1912 type have been reported in the literature. However, the eponym “Schilder’s disease” has been widely used to designate several distinct clinical and pathological disorders of the central nervous system. Myelinoclastic diffuse sclerosis, as described by Schilder in his 1912 case, is a very rare condition that needs to be differentiated from other myelin diseases, particularly adrenoleukodystrophy by specific biochemical and/or ultrastructural studies (1,2). The following case fulfills the criteria for the diagnosis of Schilder’s myelinoclastic diffuse sclerosis, 1912 type, as established by Poser et al. (2), and demonstrates its clinical and imaging dramatic response to steroid treatment.

CASE REPORT

A 14-year-old dark-skinned, right-handed girl was admitted to the hospital with a 1-month history of sudden bilateral blindness and parietooccipital headache. It had been 1.5 years since an episode of left hemiplegia with partial loss of sensation on her left side, which resolved almost completely after 19 days. At that time she also had a partial motor seizure involving the left side of her face. There was no history of preceding infection or vaccination. Previous medical history or family history for neurologic and visual disorders were negative. Physical examination on admission disclosed visual acuity was hand movements bilaterally. Ophthalmoscopic exam was normal and the pupils were 3 mm in diameter and fully reactive to light. There was a mild left hemiparesis, but no brisk or pathologic reflex could be elicited. Pinprick, light touch, vibration, and position sense were normal, as was the remainder of the neurologic examination. Routine laboratory studies including complete blood cell count, erythrocyte sedimentation rate, serum protein electrophoresis, glucose, urea nitrogen, creatinine, electrolytes,
cholesterol, lipoproteins, liver function tests, and VDRL were all normal. Urinalysis, and skull and chest roentgenograms were also negative. Lumbar puncture revealed cerebrospinal fluid with an opening pressure of 120 mm H2O. Analysis of the fluid showed 2 lymphocytes/mm3, a glucose level of 64 mg/dL, and a protein level of 71 mg/dL with 14% γ-globulin and an immunoglobulin G level of 5.2 mg/dL. Oligoclonal bands were also noted. An electroencephalogram (EEG) revealed slowing of the background activity with bursts of 3–4 cycles/s polymorphic waves on the right frontal and central areas. The computed tomographic (CT) scan (Fig. 1) revealed two roughly symmetrical hypodense lesions, with a dense ring of contrast enhancement in the occipital lobes and a smaller irregular hypodense area in the right frontal region. The right lateral ventricle was slightly increased. The presumptive diagnosis of a demyelinating disorder or a leukodystrophy was made and the patient’s adrenocortical function was evaluated. Determination of serum cortisol and urinary 17-ketosteroids and 17-hydroxysteroids showed normal values. Adrenocorticotropic hormone (ACTH) stimulation test was performed and revealed no evidence of adrenocortical failure. Conduction studies of the median, ulnar, and peroneal nerves showed normal values. A right occipital brain biopsy was then carried out. The histologic examination by Luxol-Fast Blue and silver staining techniques disclosed confluent areas of myelin disintegration. In some areas the U-fibers were also involved. The axons were less intensively affected and the cortical neurons were completely spared. Perivascular cuffs with lymphocytes and phagocytes were prominent and a large number of reactive giant astrocytes, some of them multinucleated, were found within the lesions. Small scattered areas of frank tissue necrosis and cavitation were seen. Electronmicroscopy failed to reveal any evidence of the characteristic cytoplasmic membrane-like inclusions, as were found in adrenoleukodystrophy.

The patient was treated with intravenous dexamethasone, 16 mg daily, for 1 month and then with oral prednisone in tapering doses for 3 weeks. She responded well to treatment and 30 days after starting steroid therapy she could count fingers at 50 cm from both eyes. On Goldmann perimetry there was a marked constriction of the visual fields (Fig. 2). Serial CT scans 1.5, 3, and 8 months later showed progressive reduction of the size of the demyelinating lesions and disappearance of contrast enhancement (Fig. 3). Visual acuity recovered to 20/20 bilaterally and Goldmann perimetry showed a remarkable expansion of the visual fields, remaining only a binaural inferior defect (Fig. 4). No change in the intensity of the left hemiparesis was observed.

DISCUSSION

In 1912, 1913, and 1924, Schilder described three different nosological entities (3–5) under the term “encephalitis periaxialis diffusa.” Since then a great number of articles have been published under the title “Schilder’s disease” to report cases of many other distinct disorders of the nervous system. In 1912, Schilder originally reported a case of a 14-year-old girl with mental signs and increased intracranial pressure. His clinical diagnosis was that of a posterior fossa expanding lesion that developed over a period of about 4.5 months. Surprisingly, Schilder found at autopsy two well-demarcated areas of demyelination, with almost complete sparing of the axons and the subcortical U-fibers. He considered this case a new disease of myelin that should be differentiated from brain tumors and multiple sclerosis. The following year, Schilder (4) published a postmortem study of the brain of a patient previously described by Haberfeld and Spieler (6) in 1910. He considered it a variant of encephalitis periaxialis diffusa and did not attach importance to the fact that a sibling of the patient had died of a similar disease. In 1924, Schilder reported the last of his three cases (5) con-
cerning a 37-year-old woman with a neurological disease that developed after a bout of influenza. Postmortem examination of her brain disclosed areas of diffuse demyelination and intense perivascular lymphocytic infiltrates, as well as capillary proliferation. He concluded that this case was a diffuse subacute encephalitis and included it in the group of periaxial encephalitides.

Subsequent studies on Schilder's original cases have characterized them as three different entities. His first case is now called diffuse myelinoclastic sclerosis or true Schilder's disease 1912 type (1,7). His 1913 case has been identified as adrenoleukodystrophy (8,9), whereas his 1924 report concerns what is presently known as subacute sclerosing panencephalitis (10). Much of the confusion regarding the nomenclature on Schilder's disease comes from the misuse of the terms Schilder's disease and Schilder's diffuse sclerosis to name a host of unrelated and heterogeneous conditions that have become recognized as belonging to entirely distinct categories. As a matter of fact, Schilder himself unwittingly initiated such an enormous confusion that, most unfortunately, lasts to this day. Attempts to clarify this situation soon appeared in the medical literature. In 1934, Bouman (11) reviewed 100 cases reported as Schilder's disease or Schilder's diffuse sclerosis and found only 17 cases that were in accordance with Schilder's 1912 criteria. Other disorders were harboured under these terms, such as leukodystrophies, perinatal encephalopathies, subacute sclerosing encephalitides, postinfectious perivenous encephalopathies, transitional sclerosis, and glioblastomatosis. However, it is probable that most of the 17 cases selected by Bouman as Schilder's disease 1912 type may actually represent instances of adrenoleukodystrophy (1). Poser (1,7) and Poser et al. (2) have more recently clarified the terminology and established specific criteria for the diagnosis of Schilder's myelinoclastic diffuse sclerosis 1912 type. Reviewing the literature, Poser (1) and Poser et al. (2) listed only nine published cases that can be considered as probable instances of Schilder's myelinoclastic diffuse sclerosis (12–20). They added two cases of their own that represent unquestionable Schilder's myelinoclastic diffuse sclerosis, as the diagnosis was established by biochem-
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ical and electron-microscopic examination. They concluded that most of the patients with presumed Schilder's disease reported in the literature would be better placed under the diagnoses of adrenoleukodystrophy, transitional or multiple sclerosis, or acute disseminated encephalomyelitis. Schilder's disease is a subacute or chronic myelinoclastic disorder resulting in the formation of large bilateral plaques affecting the centrum semiovale of the cerebral hemispheres. Adrenocortical function must be normal and there must be no involvement of the peripheral nerves. It may affect both children and adults of both sexes, although most of the probable and definite cases have occurred in male children. It is a diagnosis of exclusion that cannot be established exclusively on clinical grounds, neither by CT scan nor by light microscopic examination of a brain biopsy specimen. Other myelin, as well as inflammatory disorders, must be definitively ruled out. Special attention has to be paid to rule out adrenoleukodystrophy, as it may even affect girls—probably representing symptomatic carriers—and may simulate Schilder's myelinoclastic diffuse sclerosis on CT imaging and histologic preparations. Actually, in some cases of adrenoleukodystrophy there are sharply demarcated areas of myelin breakdown, with anisomorphic gliosis and intense perivascular inflammatory reaction simulating a myelinoclastic disorder. Further confusing the differentiation is the normalcy of the adrenocortical function tests in many cases of adrenoleukodystrophy. It can only be ruled out by means of analysis of the fatty-acid components of serum or brain cholesterol esters, or by the absence of the characteristic cytoplasmic inclusions on electron-microscopic study of brain or adrenal cortex.

Since these criteria for definite diagnosis of Schilder's myelinoclastic diffuse sclerosis were established, a new biopsy-proven case was reported by Sedwick et al. (21) in a 51-year-old woman with mental confusion, headache, and bilateral blindness.

The present case fulfills the criteria for the diagnosis of true Schilder's myelinoclastic diffuse sclerosis 1912 type, as has been proposed by Poser (1) and Poser et al. (2). Careful electron-microscopic examination of a brain biopsy specimen failed to reveal any cytoplasmic inclusions that would suggest adrenoleukodystrophy. In addition, oligoclonal bands were noted in the cerebrospinal fluid immunoglobulin G fraction, which was also increased. This finding has never been reported in adrenoleukodystrophy (22). A unique feature of this case was the presence of three hypodense lesions in the brain. A right frontal lobe lesion with no contrast enhancement was observed, in addition to two roughly symmetrical large hypodense areas with contrast enhancement at their edges in the occipital lobes. It is possible that the frontal lesion represented an old plaque and the occipital ones had developed more recently. This explains the left hemiparesis and the partial motor seizure that occurred 18 months preceding the visual symptoms. Steroid treatment was followed by a dramatic response both clinically and on CT imaging. The patient's vision improved from perception of hand movements to 20/20 bilaterally, with a mild binasal inferior defect on the visual fields examination. There was a progressive shrinkage of the occipital lesions to a point of almost complete disappearance, as was documented by serial CT scans. Corticosteroid therapy was followed by
marked improvement of the clinical condition in one probable (20) and in two other proven cases (1,2), but could not change the complete bilateral blindness in the case reported by Sedwick et al. (21). Reduction of the size of the lesion has been also noted in two previous cases (1,2).

Although it is an extremely rare condition, true Schilder’s myelinoclastic diffuse sclerosis 1912 type must be included in the differential diagnosis of acute neurological deficits, particularly when visual loss occurs and bilateral large hypodense lesions are observed on CT scan. Appropriate workup may establish the correct diagnosis.

REFERENCES
Schilder's Disease and Adrenoleukodystrophy

The article by Drs. Lana-Peixoto and dos Santos on “Schilder’s myelinoclastic diffuse sclerosis” in this issue of the Journal of Clinical Neuro-ophthalmology describes a very interesting neuro-ophthalmic problem seen in a 14-year-old young girl in Brazil. It has been recognized in recent years that the entity formerly called Schilder’s disease in the literature represented the condition more recently defined as adrenoleukodystrophy. Dr. Lana-Peixoto’s paper was kindly reviewed by Prof. Hugo W. Moser of Johns Hopkins University, one of the world authorities in pediatric leukodystrophies. Dr. Moser wrote in his review, “This interesting paper shows a striking favorable response to steroids in a 14-year-old girl with presumed Schilder’s myelinoclastic diffuse sclerosis. As the authors note, the major differential is from adrenoleukodystrophy. Adrenoleukodystrophy is made much less likely by the patient’s female sex, normal adrenal function, and absence of electron microscopic inclusions. However, to rule out adrenal leukodystrophy beyond doubt, very long chain fatty acids should be studied in plasma and cultured skin fibroblasts.”

Dr. Moser volunteered to do these special studies—i.e., measuring long chain fatty acids in plasma and cultured skin fibroblasts—in his laboratory. He thought the CT scan was highly compatible with adrenoleukodystrophy and that the tests done did not rule it out unequivocally. We therefore wrote the authors in Brazil and made these suggestions. However, Dr. Lana-Peixoto wrote back that they have been trying to get in touch with the patient without success. She moved away to the countryside, and no response to a telegram at her new address was received. Dr. Lana-Peixoto humbly suggested that if the paper could be published without data concerning plasma very long chain fatty acids—as actually almost all accepted cases of Schilder’s disease had been—he would appreciate it, and if the patient could be localized and a plasma analysis obtained, an addendum or supplementary letter to the editor would be sent. That seemed reasonable, and therefore this interesting case has been published. It is believed that the correspondence and workup suggestions would be helpful to the clinician seeing a case with a similar differential diagnosis. The action behind the scenes often supplements the original reports, I believe!

Dr. Fishman recently brought to my attention an 11-year-old boy who had experienced a rapid drop of vision in both eyes at age 6 in Chicago and showed an unusual pigmentary retinopathy. He had apparently remained normal, except for being legally blind, until December 1988, when he developed generalized seizures. The patient was seen by Dr. John Susac, an editorial board member of this Journal. It appeared clinically likely that the boy had a form of cerebromacular degeneration. When considering such formidable studies as brain biopsy, rectal muscle or sural nerve biopsy or the like, Dr. Susac suggested the simple expedient of looking at a stained peripheral blood smear on the boy. This was done and immediately revealed abnormal lymphocytes with cytoplasmic vacuoles and granules. This allowed the diagnosis of neuronal ceroid lipofuscinosis (Batten-Vogt's disease) to be made in this young boy without additional and more unpleasant and expensive studies being necessary. An excellent chapter/review on that syndrome is chapter 27, “Neuronal ceroid lipofuscinosis (Batten-Vogt's disease),” on pp. 299–317 of “Neuro-ophthalmology Focus 1982,” Masson Publishing Co., New York, written by Drs. Scott Jaben and John T. Flynn and edited by the undersigned. On page 308 of that article are two nice light microscopic smears showing vacuolated lymphocyte and azurophilic hypergranulated polymorphonuclear leukocyte from a patient with this disease. The reason this reference is cited is that these cases are quite rare in practice, and it helps the clinician seeing such cases to remember to send plasma on a case of suspected Schilder’s disease up to Dr. Moser, and to simply check a peripheral blood smear on a child with a suspected cerebromacular degeneration, as both may be extremely helpful in pinning down these difficult diagnoses.

J. Lawton Smith, M.D.
Editor
Palinopsia as a Presenting Manifestation of Creutzfeldt-Jakob Disease

Valerie Purvin, M.D., Jose Bonnin, M.D., and Julius Goodman, M.D.

A 70-year-old man developed a syndrome of progressive nondominant parietal and occipital dysfunction including palinopsia and a visual field defect. Despite the marked focality of his clinical findings, radiologic studies were normal. Myoclonus and ataxia began 6 weeks after onset of his illness at which time brain biopsy confirmed Creutzfeldt-Jakob disease (CJD). This is the first reported case of palinopsia due to CJD.

Key Words: Palinopsia—Creutzfeldt-Jakob disease (CJD)—Dementia.

Palinopsia is a rare disorder of visual perception characterized by persistence of an image after removal of the exciting stimulus. Such images usually persist for several minutes, although occasional cases may last for hours or days. Palinopsia often becomes evident early in the course of a progressive hemianopic visual field defect and may resolve as the defect becomes complete (1). Other abnormalities of visual perception such as illusory motion, distortion of size and shape, and transposition of objects in space are frequently present (2). Most reported cases are due to a structural lesion in the nondominant parietooccipital area. We report a patient in whom vivid palinopsia was the initial manifestation of Creutzfeldt-Jakob disease (CJD).

CASE REPORT

A 70-year-old right-handed man was in good health until June 1987, when he noticed problems with reading. Specifically, he described abnormal persistence of visual images. One example of this occurred when he looked at a mustard jar and then at a piece of bread. He believed the bread had become moldy until he realized he was still seeing the green label from the mustard. Palinoptic images lasted from minutes up to an hour, and each image did not recur after its resolution. Images were not confined to a particular area of the visual field. Perception of these images was not associated with any alteration of consciousness or focal neurologic deficits. He also noted problems reading, which he attributed to a “missing portion” in the center of each word. Over the next 4 weeks, he experienced a variety of other visual distortions, illusions, and hallucinations. On one occasion, a moving car appeared to him to be 6 inches off the ground. On another occasion, every building he
looked at appeared to have a "bite" taken out of the roof. He denied language difficulty, numbness, weakness, headache, fatigue, weight loss, or any other constitutional symptoms. Past medical history included essential hypertension and a balloon angioplasty in 1985.

Ophthalmologic examination revealed a visual acuity of 20/50 in each eye with normal pupillary responses. On testing with Ishihara pseudoisochromatic plates, he was able to identify only the screening plate in each eye. Goldmann perimetry (Fig. 1) revealed an absolute left homonymous hemianopic scotoma and a smaller homonymous central defect to the right of fixation. Ocular motility was normal as was a dilated fundus exam.

On neurologic testing, he was alert and attentive and was oriented to person, place, and time. He recalled two of three items at 5 min. Verbal output was fluent and grammatically correct with intact repetition. He followed two-step commands easily but had mild difficulty with more complex instruction. There was no anomia, he was able to name colors correctly, and there was no right-left confusion. He had difficulty with serial subtraction. There was marked constructional apraxia with failure to close each of his figures. He extinguished the left hand on simultaneous stimulation. Tone, strength, and coordination were intact. There was mild flattening of the left nasolabial fold; cranial nerves were otherwise intact.

A complete blood count, chemistry profile, erythrocyte sedimentation rate, VDRL, fluorescent treponemal antibody (FTA), serum protein electrophoresis, urinalysis, chest x-ray, and EKG were normal or negative. Computed tomographic (CT) scan of the head before and after intravenous contrast infusion was normal except for mild ventricular enlargement. A magnetic resonance imaging (MRI) scan contained some motion artifact but revealed no abnormalities. An EEG was generally slow especially posteriorly with no paroxysmal discharges.

Two weeks after his initial presentation, he reported increased visual difficulty, dressing apraxia, and spatial disorientation. His family also described occasional brief jerking movements of the extremities more frequent on the left side. Examination revealed marked progression of his left homonymous hemianopsia with some worsening of the right hemi-field defect (Fig. 2), abnormal posturing and dysmetria of the left upper extremity, mild gait instability, and left astereognosis and agraphesthesia. There was again no evidence of aphasia. CSF exam and three-vessel angiography were normal.

To confirm the clinical suspicion of CJD, a brain biopsy was performed. A 1-cm$^3$ sample taken from the right parietal cortex was examined by light and electron microscopy. The neuropil had marked spongiform change with many small, primarily...
rounded or oval vacuoles in the deeper cortical layers. Ultrastructurally, the vacuoles could be localized in the cell bodies and processes of neurons and astrocytes. There was also a moderate loss of neurons, and some of the remaining ones had large vacuoles that distended the cell bodies and compressed the nuclei. Reactive proliferation of the astrocytes was also a prominent feature. The triad of spongiform change, neuronal loss, and astrocytosis is characteristic of CJD. The diagnosis was further supported by some negative observations such as the absence of an inflammatory reaction, infiltration with macrophages, necrosis, or the morphological hallmarks of any dementing process.

The patient continued his rapid neurologic decline. Seven weeks after initial onset of his illness, he was lethargic, unable to stand, and displayed frequent diffuse myoclonic jerks. EEG at this stage showed marked slowing with periodic spike and sharp wave discharges over the right posterior region.

He was transferred to a nursing home where he died 1 week later. An autopsy was not performed.

DISCUSSION

The pathophysiology of palinopsia is not yet fully defined. There is probably more than one form of the disorder. In some cases, palinopic images occur episodically, recur at some time after the initial event, and respond to anticonvulsants. Such cases probably represent a form of sensory seizure (3,4). In other cases, there is evidence of prolongation of the normal afterimage (5,6). Such prolongation may be selective for specific stimulus parameters such as shape, color, and duration (6). In the majority of cases, there is no evidence of altered physiologic afterimage. The mechanism in these instances may be loss of normal inhibition of visual-memory pathways, thus creating an "uninhibited reverberating circuit" (2).

Most cases of palinopsia have been associated with a focal lesion in the nondominant parietooccipital area (1), although rare cases have involved the posterior left hemisphere (1,5,7) or more anteriorly placed lesions (1,8). Specific causes have included tumor (1), ischemia (9), trauma (5), arteriovenous malformation (3), migraine (10), and abscess (11,12). In rare instances, no structural lesion is found, including cases of carbon monoxide poisoning, drug intoxication (13), and one case in which cerebral vasculitis was suspected (6).

In our case, palinopsia was the presenting manifestation of CJD. A variety of different visual abnormalities have been described in patients with CJD. Nonspecific complaints of blurred or dim vision are common (14). Higher cortical visual disturbances including visual distortions, dyschromatopsia, visual agnosia, and micropsia have also been reported (15). Homonymous hemianopic visual field defects are sometimes suspected, but formal perimetry is usually not feasible due to declining intellect and attention. In some cases, a hemi-
anopic defect is impossible to distinguish from hemiattentiveness due to parietal lobe dysfunction. In more advanced stages, cortical blindness (loss of vision with normal pupils and optic discs) is frequent. Ocular motility disturbances are less common and include supranuclear (16) and infranuclear palsies (15), ptosis (15), and apraxia of eyelid closure (17).

Variability in the clinical and pathologic manifestations of CJD has led to attempts to divide the disorder into subgroups including one form with prominent visual manifestations. This entity was first described by Heidenhain in 1929 (18). He described three patients with a dementing disease, the course and histology of which were compatible with CJD. Two of these patients had cortical blindness as a prominent finding, and in these cases autopsy revealed the most severe changes in the occipital cortex. A similar case was reported in 1954 by Meyer et al. (19) who proposed the term "Heidenhain syndrome." The subject of this report had "failing vision," normal appearing optic nerves, and a possible right homonymous hemianopic defect. Two similar cases were described by Jones and Nevin (20), who believed this condition was vasculopathic in nature and proposed the term "subacute vascular encephalopathy." In 1967, Nevin (21) reviewed 102 cases gathered from the literature or studied personally. Based on clinical and pathologic features, he differentiated between cases of CJD and an entity he called "subacute spongiform encephalopathy" (SSE), the latter category containing cases of the "Heidenhain variant" of CJD. According to his schema, SSE is distinguished clinically from CJD by its later age of onset, more rapid progression and paucity of upper and lower motor signs in SSE. Pathologically cases of CJD show focal involvement of frontal and temporal regions, whereas SSE cases exhibit more diffuse changes with particular occipito-parietal predominance. Siedler and Malamud (22) reviewed a total of 72 cases and came up with a similar classification but felt that these subgroups did not constitute two different diseases. The basis for diverse expressions of an apparently identical pathogen remains obscure. Factors that might influence disease expression include age at which infection occurs, route of entry, and differing strains of infectious agents (23).

Although some degree of asymmetry is common early in the course of CJD, marked or prolonged predominance of signs and symptoms referable to one area of the brain is rare. Two recent reports describe patients with CJD affecting the left hemisphere preferentially. One patient, a 61-year-old man, had progressive, isolated aphasia for ~1 year before the onset of a fatal dementing illness with typical features of CJD (24). Another, a 73-year-old woman, presented with right hemiparesis, deteriorated rapidly to somnolence, and died 8 weeks after onset (25). Autopsy showed typical changes of CJD affecting the left hemisphere with only minimal abnormality of the right hemisphere.

Our patient's initial complaint was palinopsia, suggesting a lesion of the left occipitoparietal area. Neurologic examination revealed a congruous left hemianopic defect compatible with a right occipital lesion. He also exhibited constructional apraxia and left-sided extinction indicating right parietal lobe involvement. He subsequently experienced progression of the hemianopic visual field defect and more severe nondominant parietal dysfunction before developing evidence of widespread involvement including myoclonic jerks, rigidity, and dementia.

Our patient represents an example of the Heidenhain variant of CJD. Typical features include the patient's advanced age, rapid progression, and absence of motor signs. In addition to the characteristic predominance of occipital and parietal dysfunction, our patient also exhibited preferential involvement of the right hemisphere with striking preservation of dominant hemisphere function. This occurrence is consistent with the concept of CJD as a multifocal rather than diffuse degenerative disease (26). A notable feature was the presence of focal clinical findings and the absence of focal change on CT, MRI, and angiography. Focal findings with normal radiologic studies should suggest the possibility of spongiform encephalopathy.

REFERENCES

Creutzfeldt-Jakob Disease and the Ophthalmologist

Purvin et al. (1) describe a patient in whom palinopsia was the presenting symptom of Creutzfeldt-Jakob disease, and this adds another neuro-ophthalmological manifestation to the list of visual and oculomotor disturbances encountered in this mysterious malady that usually begins in the second half of life with one of the following presentations: (a) Dementia, concomitant pyramidal, and extrapyramidal signs are frequently found. (b) Cerebellar ataxia. Various ocular motility disturbances can be detected; vertical supranuclear gaze palsy has been reported (2) and also observed by us as an initial manifestation. (c) Visual cortical disturbances. Field defects and visual agnosia may progress to cortical blindness. The case reported in this issue belongs to this form, also named the Heidenhain variant.

Whatever the initial manifestations, within several weeks or months the patient’s condition deteriorates rapidly to a state of akinetic mutism; widespread myoclonic jerks appear, and the electroencephalogram shows characteristic periodic discharges of triphasic waves every 1–2 s, mistaken occasionally for electrocardiographic artifacts. Most patients die within 10 months, but a fulminant course of a few weeks is no rarity.

Microscopic examination of the brain reveals neuronal loss, astrocytosis, and the characteristic spongy degeneration, consisting of intracellular vacuoles, especially in the gray matter. Similar pathological changes are found in some other diseases, collectively termed spongiform encephalopathies. The important representatives are scrapie in sheep and kuru and Creutzfeldt-Jakob disease in humans. “Subacute spongiform encephalopathy” described by Nevin et al. (3) and attributed by them to ischemia is regarded as identical with Creutzfeldt-Jakob disease (4).

Veterinarians observed that scrapie can be transmitted to other sheep with long incubation periods of about a year and introduced the term “slow virus infection,” also characterized by the absence of inflammatory and immune responses (5).

The first human disease proved by Gajdusek et al. (6) to be of this kind and transmitted to chimpanzees was kuru, endemic in New Guinea and having the unusual mode of transmission by ritual cannibalism of the deceased. Creutzfeldt-Jakob disease, regarded then as a degenerative disease, was transmitted to chimpanzees in 1968 (7). Gajdusek received the Nobel prize for his achievements in 1976.

The transmissible agent, though previously referred to as “slow virus,” actually did not show features of a virus. It is resistant to conventional methods of sterilization including boiling, regular autoclaving, ultraviolet light, Lysol, tincture of iodine, and prolonged exposure to formalin. Moreover, it is composed of protein and does not contain nucleic acids, DNA, or RNA. Prusiner coined the name “prion” for these proteinaceous infectious particles (8–10). The idea of infectious proteins is quite revolutionary; it remains to be explained how the prion replicates without nucleic acids. Even more perplexing is that the prion protein is probably an abnormal isofrom of a protein found normally in cell membranes. The gene coding the protein has been compared to an oncogene.

The incidence of Creutzfeldt-Jakob disease worldwide is about one per million. An exceptionally high incidence of 31 per million exists among Libyan-born Jews who have immigrated to Israel (4,11). They also have high familial clustering (12). Awareness of the disease in Israel is such that practically every Libyan patient with unspecified progressive neurological disease is suspected to harbor it. Genetic susceptibility may be the explanation for the high incidence and familial clustering. A relatively high incidence has also been re-
ported among immigrants from North Africa to France, but the situation in Libya itself and in other North African countries is unknown.

The natural mode of acquisition of the disease is unknown. There is no convincing evidence for person-to-person transmission, and there is no proof of environmental factors such as exposure to scrapie. Iatrogenic transmission is well documented by corneal transplantation (13,14), intracerebral electrodes (15), and possibly by cadaveric dura mater grafts (16). Children treated with growth hormone extracts from cadaveric pituitary glands manifested signs of Creutzfeldt-Jakob disease decades thereafter (17). Consequently, no corneal or any other transplants should be taken from patients dying with dementia of uncertain cause. It has been suggested that the disease might even be transmitted by a tonometer measuring intraocular pressure (18). Previous trauma to the head and neck and operations have been listed as possible risk factors, probably by activating the dormant infectious agent (18). The balloon angioplasty that the patient of Purvin et al. underwent 2 years prior to his illness may thus be relevant.

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REFERENCES


Dolichoectasia and Cranial Nerve Palsies
A Case Report

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An elderly man with glaucoma and acute onset of left-sided cranial nerve III, V, and VII palsies was found to have associated marked intracranial artery dolichoectasia. Dolichoectasia (arterial elongation and distension) affects the intracranial arteries, producing various neurological and ophthalmological findings. The patients are usually men who are more than 40 years old and have a history of hypertension. Diagnosis is made by characteristic radiologic findings. In patients with neurologic symptoms and signs suggesting a space-occupying mass, intracranial dolichoectasia should be considered.

Key Words: Dolichoectasia—Cranial nerve palsies—Glaucoma.

Dolichoectasia (dolichos, long; ectatic, distended) is a distinct disease entity affecting the arteries which may present clinically as an intracranial space-occupying lesion (1). Multiple reports of cranial nerve palsies (III-XII) associated with dolichoectatic intracranial arteries are found in the nonophthalmological literature (1-10), but a recent search revealed only one such report (using different nomenclature) noted in the ophthalmology literature (11).

We report a case in which a patient experienced an acute onset of left-sided third, fifth, and seventh cranial nerve palsies associated with marked intracranial dolichoectasia.

CASE REPORT

A 74-year-old white man with a long-standing history of hypertension, alcoholism, and primary open angle glaucoma was being followed in the eye clinic for glaucoma, when a rise in intraocular pressure associated with progression of visual field loss was noted in both eyes. The patient was scheduled for a laser trabeculoplasty, but in the interim he presented to an otolaryngologist with left-sided otalgia and otorrhea, which were diagnosed as symptoms of otitis externa. At that visit (which was 11 days after his last eye exam) the patient complained of diplopia and instability when walking. The patient denied any past history of diabetes or symptoms that would suggest giant cell arteritis. Re-examination of the patient revealed a marked limitation of the left eye in supraduction and adduction and a slight decrease in infraduction (Fig. 1 top). Abduction was normal, as was incycloduction in downgaze. Marked ptosis on the left was also apparent. Pupillary involvement was indeterminate because the patient was using 4% pilocarpine drops. Decreased corneal sensitivity was also noted on the left and hyperesthesia was found over the left brow and cheek. No
definite seventh nerve involvement was noted by voluntary muscle contraction, although the patient had a slightly asymmetric facial appearance with some loss of skin lines on the left. No proptosis was noted. Because of the apparent involvement of cranial nerves III, V, and VII, a computed tomographic (CT) scan was obtained to rule out an inflammatory or infectious process of the petrous area, orbit, and/or cavernous sinus versus an aneurysm.

The CT scan showed clear sinuses, a probable old right medial orbital wall fracture, but no evidence of a mass lesion in the region of the left cavernous sinus or orbital apex. However, there was dolichoectasia of the great cerebral vessels, including the right vertebral artery, basilar artery, and both carotid arteries. The basilar artery bifurcation was noted to be markedly elevated, lying at the level of the midportion of the third ventricle on the left. There was marked leftward displacement of the medulla by the enlarged tortuous right vertebral artery (Fig. 2). No evidence of a focal aneurysm was noted and the lesion was felt to be inoperable.

Magnetic resonance imaging (MRI) was also obtained, which again showed marked tortuosity of the basilar artery, with its tip indenting the hypothalmus (Fig. 3). The cerebral peduncles were displaced superiorly and dorsally, and the third nerves appeared to be stretched, particularly on the left (Fig. 4). Enlargement of the carotid arteries was also noted.

One week later the patient was again seen with a marked seventh nerve palsy on the left, in addition to a persistent third and fifth nerve weakness (Fig. 5). The Department of Neurosurgery at The Oregon Health Sciences University was consulted, but no treatment or further imaging (including an-

FIG. 2. This axial CT image of the midposterior fossa at the junction of the pons with the brainstem shows enhancement in the right vertebral and carotid artery, and the dilated basilar artery.
DOLICHOECTASIA AND CRANIAL NERVE PALSIES

FIG. 3. This coronal T-1 weighted MRI image shows marked tortuosity of the vertebro-basilar vessels (arrows) with indentation of the hypothalamus (star).

giography) was advised. Therefore, no cerebral angiogram was obtained.

Six weeks after the onset of his diplopia, much less ptosis was evident and marked improvement of the extra-ocular muscle movement was noted. Approximately 3 weeks later, the patient returned for followup with no further complaints of diplopia. Extra-ocular muscle movements were full (Fig. 1 bottom), and only a slight ptosis and facial droop remained (Fig. 6). Also, no paresthesia or hyperesthesia was noted over the distribution of cranial nerve V.

Followup since that time has been sporadic, with poor patient compliance and refusal of the patient to see a neurologist for further workup. However, blood glucose was found to be within normal limits (98). Blood pressure was last noted to be elevated at 160/104, and the Department of General Medicine is continuing to follow the patient for hypertension.

DISCUSSION

Dolichoectasia (elongation and distension) of the arteries is an uncommon condition (3,7,12,13) that may affect the intracranial arteries. Yu et al. (7) noted the rarity of this condition when reviewing ~50,000 carotid and vertebral angiograms performed in Queen Square, London, England from 1959 to 1980. Of these, only 29 cases demonstrated unequivocal arterial ectasia. In another report, Nijensohn et al. (3) found 23 patients diagnosed with basilar artery ectasia among all autopsies performed from 1952 to 1972 at the Mayo Clinic, Rochester, MN, U.S.A.

First termed dolichoectasia in 1969 (1), this condition is considered by some to be a distinct disease entity. Sacks and Lindenburg (1) studied the histopathology of the affected arteries and found gaps in the internal elastic membrane and thinning of the media, which suggested a degenerative process. The same authors noted that dolichoectasia can occur without evidence of arteriosclerosis and they proposed that the disease may actually be present for many years without clinical symptoms. They speculate that stress, such as high blood pressure, may further enlarge the arteries and produce symptoms that suggest an intracranial mass. Other authors (2,7) describe the anomaly as being most common in males >40 years old and as being found in association with hypertension (7,13).

The clinical picture of dolichoectasia of the intracranial arteries can be quite varied. Boeri and Passerini (2) noted the frequent presence of an extensive third cranial nerve paresis on the side corresponding to the convexity of the curve of the artery. In addition to multiple cranial nerve palsies (1-10), symptoms and signs associated with dolichoectasia of intracranial arteries include retinal ischemia (7), hydrocephalus (7,10,14), chiasmal compression (7), headache (6), tinnitus (6), hemiparesis (6), paresthesias (6), trigeminal neuralgia (9,15), seizure (12), senile dementia (14), papilledema (13), nystagmus (13), ataxia (13), isolated envi-
FIG. 4. In this axial proton density MRI image of the midposterior fossa, the bright signal evident is slow-flowing blood in the right vertebral artery (arrow) with marked indentation of the brainstem. Note the convexity of the curve is on the side of the clinical findings.

ronmental tilt (16), and hemifacial spasm (10,17). A finding in the evaluation by Smoker et al. (10) of 22 patients diagnosed with isolated hemifacial spasm deserves special emphasis: vertebrobasilar dolichoectasia was demonstrated by CT in all of their 22 cases.

The diagnosis of dolichoectasia of the intracranial arteries is determined by radiologic findings (2,10,13,17–22). Numerous measurements can be made using angiography that correspond closely to autopsy data (2). However, characteristic CT findings are considered diagnostic, making invasive procedures unnecessary in many cases (10,13). MRI has also been used (16).

The prognosis of dolichoectasia varies. In one report (7) mortality (defined as death in followup period ranging from 1 month to 17 years) for ca-

FIG. 5. Note marked left-sided ptosis and facial droop consistent with cranial nerve III and VII palsies.

FIG. 6. Six weeks after onset, much less ptosis and facial asymmetry are evident.

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REFERENCES

Bilateral Internuclear Ophthalmoplegia Associated with Fourth Ventricular Dermoid Tumor

Ismail H. Tekkok, M.D., Giyas Ayberk, M.D., Tulay Kansu, M.D., and Suleyman Saglam, M.D.

We report an unusual case of bilateral internuclear ophthalmoplegia occurring in association with fourth ventricular dermoid tumor and we review the current literature.

Key Words: Bilateral internuclear ophthalmoplegia—Dermoid tumor—Fourth ventricle.

Bilateral internuclear ophthalmoplegia results from bilateral lesions of the medial longitudinal fasciculi and is usually considered to be a pathognomonic sign of demyelinating disease (1). However, many other causes have been defined in recent years. To our knowledge, our case report is the only one in the literature published in English that shows an association with a fourth ventricular dermoid tumor (Table 1) (2–23).

CASE REPORT

A 7-year-old girl presented with unsteady gait and impairment of her vision. She was known to be late in reaching her developmental stages. Her unsteadiness had been profound for the last 2 years and she had been vomiting quite frequently for ~6 months before admission. Her teacher observed a progressive impairment of her concentration during the last 3 months. She was always complaining of headaches and neck pain.

On admission her head circumference was 54.5 cm. She was fully alert, cooperative, and had no disorientation. Neurological examination revealed limited adduction bilaterally. Nystagmus was present in all directions; it was most marked with lateral gaze and in the abducting eye. Her visual acuity was 20/25 bilaterally and the visual fields were full on confrontation. Funduscopic findings were normal. Facial sensation and corneal reflex were diminished bilaterally. She had minimal left-sided facial paresis.

Gag reflex and other lower cranial nerve functions were normal, as well as the power, tone, and sensation in her limbs. The cerebellar functions were impaired, most markedly on the left. Gait was ataxic, and she had a tendency to fall to left.
TABLE 1. Summary of previously reported causes of bilateral internuclear ophthalmoplegia

<table>
<thead>
<tr>
<th>Cause of BIND</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spino-cerebellar degeneration</td>
<td>Weiner et al. 1967 (2)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>Henishanu and Lavy, 1969 (3)</td>
</tr>
<tr>
<td>Brainstem tumors</td>
<td>Cogan and Wray, 1970 (4); Fotzsch, 1971 (5)</td>
</tr>
<tr>
<td>Occlusive cerebrovascular disease</td>
<td>Wallace &amp; Culebras-Fernandez, 1970 (6); Gonyea, 1974 (7)</td>
</tr>
<tr>
<td>Neurophilis</td>
<td>Cogan, 1970 (8)</td>
</tr>
<tr>
<td>Arnold-Chiari malformation with hydrocephalus</td>
<td>Cogan, 1970 (8); Nishikazi et al., 1985 (9)</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>Gonyea and Heilman, 1972 (10)</td>
</tr>
<tr>
<td>Angiokeratoma corporis diffusum (Fabry’s Disease)</td>
<td>Schmidt and Zimmerman, 1973 (11)</td>
</tr>
<tr>
<td>Head injury</td>
<td>Rich et al., 1974 (12); Baker, 1979 (13); Beck and Meckler, 1981 (14), Keane, 1987 (15)</td>
</tr>
<tr>
<td>Branchial cyst</td>
<td>MacDonald and Sher, 1977 (16)</td>
</tr>
<tr>
<td>Subdural hematoma</td>
<td>Deveaux et al., 1979 (17)</td>
</tr>
<tr>
<td>Basilar artery aneurysm</td>
<td>Deveaux et al., 1979 (17)</td>
</tr>
<tr>
<td>Fourth ventricular epidermoid tumor</td>
<td>Schraeder et al., 1981 (18)</td>
</tr>
<tr>
<td>Carcinomatous meningitis</td>
<td>Ford et al., 1983 (19)</td>
</tr>
<tr>
<td>Narcotic overdose</td>
<td>Rizzo and Corbetti, 1983 (20)</td>
</tr>
<tr>
<td>Meningoencephalitis</td>
<td>Bodzin et al., 1983 (21)</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>Donhowe, 1984 (22)</td>
</tr>
<tr>
<td>Tuberculosis granuloma in midbrain</td>
<td>Inosencio and Baleecker, 1985 (23)</td>
</tr>
</tbody>
</table>

* BIND, Bilateral internuclear ophthalmoplegia.

The plain skull x-rays showed digital impressions. A computed tomographic (CT) scan demonstrated a cystic tumor within the fourth ventricle that distorted the brain stem forwards and obstructed the CSF passageways, hence causing triventricular hydrocephalus (Fig. 1). Results of routine laboratory tests were found to be within the normal range.

A suboccipital craniectomy was performed on March 22, 1988 with the girl in the sitting position. The vermis portion of the cerebellum was hypoplastic with a bulging midline lesion. Small cheesy particles were flowing freely in the cisterna magna. The surface of the tumor was also cheesy and fragile and could be easily cleaved from the cerebellar hemispheres. It was about 6 cm in diameter. The central part of the tumor was quite solid. As soon as the tumor was separated from cerebellar hemispheres, it fell off (Fig. 2a,b). There was only one feeding vessel coming from the anterior aspect. The CSF passageway was then free of obstruction.

The postoperative period was uneventful. On the fifth postoperative day her ophthalmoplegia was significantly improved and her gait was more steady. The histopathological diagnosis was a dermoid tumor (Fig. 3). A postoperative CT scan showed no residual tumor (Fig. 4).

**DISCUSSION**

Dermoid tumors account for 0.1-0.7% of all intracranial space-occupying lesions; they arise from displacement of epithelial tissue early in the intrauterine life. Dermoids are more frequent in children and the middle-aged (24). Their rate of increase in size is slow and the clinical course of the disease is rather swift, especially for dermoids occurring within the posterior fossa, where the average duration of symptoms is <1 year (24). Only a limited number of fourth ventricular dermoids have been reported in large series (24,25). None of these cases reported bilateral internuclear ophthalmoplegia, as exhibited in our patient. The vast majority of other fourth ventricular tumors reported in the literature to have bilateral internuclear ophthalmoplegia were malignant, i.e., medulloblastomas (4,5) and a choroid plexus papilloma (5), whereas only one case of a benign tumor was reported in 1981 to exhibit bilateral internuclear ophthalmoplegia, which was histologically confirmed as an epidermoid (18).

Although the mechanism of bilateral internuclear ophthalmoplegia in the presence of an extrinsic lesion is far from clear, it is best explained by the stretching of the basilar paramedian arteries resulting in selective ischemia of the medial longitudinal fasciculi and/or actual brainstem compress-
sion (3,6). The rapid return to normal eye movements in our patient supports the view that brainstem compression was the cause of bilateral internuclear ophthalmoplegia.

FIG. 2. A and B: Peroperative photograph showing complete removal of the tumor.

FIG. 3. Photomicrograph of the tumor specimen showing skin appendages and a hair follicle (arrow). Hematoxylin and eosin stain. x148.

FIG. 4. Postoperative CT-scan showing no residual tumor.

REFERENCES

17. Deveraux MW, Brust JCM, Keane JR. Internuclear ophthalm-
Optokinetic Nystagmus
A Clinical Review

Noble J. David, M.D.

Although optokinetic nystagmus was described as a clinical phenomenon over 150 years ago, its neurophysiologic mechanism has provoked ongoing controversies and enthusiasm for its clinical application has been sporadic and tepid. In the past 15 years, improvements in clinical and experimental oculography, neuroanatomy, and single unit neuron recordings in alert animals have helped to resolve the neural circuitry of optokinetic nystagmus and to better define its clinical usefulness. The writer reviews the history of the experimental study of optokinetic nystagmus and the clinical circumstances in which this office test may be of particular value.

Key Words: Optokinetic nystagmus—Saccades.
of passengers on a train watching the passing scenery. The development of an instrument to test the phenomenon, the optokinetic drum, led Barany (6) to study patients and note the asymmetry of optokinetic responses in patients with homonymous hemianopsia, erroneously ascribing the abnormality to sensory impairment. On the other hand, Ohm (7) soon found quite normal optokinetic nystagmus in both directions in patients with dense and complete homonymous hemianopsia; these observations led to the convention of naming hemianopsia either of the Barany or Ohm type depending on whether or not there was an abnormal or normal optokinetic response. In any case, the deficient response was typically seen when targets were taken out of the hemianopic field and towards the damaged hemisphere. I review the evidence for localization and significance of this asymmetry later.

That the optokinetic response occurs involuntarily when the patient looks at a succession of targets can easily be proven by doing the test on your colleague. The subject is not aware of eye movements nor can she or he easily suppress the response. That these eye movements also occur as an involuntary response when targets are moved before the eyes of animals, who cannot be instructed to look, is a well-known fact that has been used to test the visual acuity of animals and that originally led to experiments aimed at clarifying the neurologic circuits involved.

In humans, we must await the vagaries of disease to produce the propitious lesions. Students of optokinetic nystagmus were early attracted to the study of experimental animals because they may be precisely lesioned and then tested. Such experiments began more than 60 years ago. The work of terBraak (8), published in 1936, is regarded as seminal. His observations established the following facts.

1. That in all experimental animals, including those who had no foveal vision, optokinetic response could be induced by movement of the entire visual field, such as the stimulation produced by an animal within an illuminated rotating striped drum.
2. Afoveate animals did not respond to the movement of small targets in the visual fields as would cats, dogs, and primates, that is, animals with foveal vision, whose attention could be attracted to a succession of moving targets progressing horizontally against a stable visual background.
3. terBraak (8) distinguished these two types of nystagmus as so-called active nystagmus for the foveal tracking of a succession of small targets, and passive nystagmus to the phenomenon seen when the entire peripheral visual field was moved. This distinction is important in the neurophysiology of optokinetic nystagmus. The "active" type of nystagmus seems to depend very much on cortical vision and is most highly developed in the primates and in humans. It is the type most easily impaired when cortical vision is destroyed by occipital ablation. That optokinetic nystagmus can persist in a decorticate cat or dog, and certainly in the rabbit, is rather difficult for a clinical neurologist to accept. But this "passive" optokinetic nystagmus seems in these animals to be mediated at subcortical level by pathways that do not involve cortical vision but which lead directly from the lateral geniculate to the tectal areas and thence to the optomotor centers of the cerebellum and brain stem.

**"ACTIVE" VERSUS "PASSIVE" OPTOKINETIC NYSTAGMUS**

Moreover, there are important distinguishing characteristics of the eye movements, particularly the slow-phase movements, in the two different pathways for the generation of optokinetic movements (2). The nystagmus produced by the subcortical pathway shows a very slow build-up in the velocity of the slow phase of the response, which reaches a maximum and reverses into an "after-nystagmus" in the opposite direction when the rotation of objects in the peripheral field is stopped. In contrast, the cortical or "active" nystagmus induced by a succession of foveal targets in motion as seen in primates and humans as well as lower animals with foveal vision locks in at full velocity when it begins and is not followed by after-nystagmus. In cats and dogs, the two types of optokinetic response are virtually separable in that the "passive" type will persist after the occipital lobes are removed. In primates and humans, it is likely that enough of both systems have been incorporated into the posterior cerebral hemispheres so that both types, though utilizing separate pathways for some of their circuitry, are virtually destroyed if the occipital lobes are removed.

One is inclined to theorize teleologically that, although the afoveate animals, whose experimental prototype is the rabbit, are generally vegetarian grazers whose chief concern is to escape detection and slaughter, their vertebrate cousins, cats and dogs, are primarily carnivores, whose macular inspection of potential prey moving across the visual field is crucial to survival [and to "active" optiki-
nestic nystagmus (OKN)]. They must pick out an animal scurrying across the landscape, perhaps one of a herd, and then hold the quarry in clear perspective until it can be overtaken and killed. In primates with highly discriminative cortical vision, the optokinetic function seems to be taken up entirely as a cortically mediated activity, providing for a roaming visual search of the environment to assist in feeding and reproductive chores. In this scheme of "active" optokinetic nystagmus provoked by foveal vision, it should be remembered that the object of regard is moving across a stable peripheral visual environment, in contrast to the "passive" OKN stimulated by movement of the entire visual environment.

Important differences in humans and experimental animals must be kept in mind when testing OKN and comparing their responses. Humans can be given verbal instructions and asked to direct visual attention to small moving targets. In all fairness, it must also be said that when small targets are moved in the direct line of vision, it is very difficult for humans not to look at them. Animals cannot talk. They must be relied upon to respond instinctively to the moving visual scene, and this often requires stimulation of much or all of the peripheral retina fields as well as central. Experimental ablation in the CNS may be freely studied in animals. In humans, we must await the vagaries of disease to produce the proper lesions for study. Notwithstanding the conditions stated above, it is obvious that animals can retain their optokinetic responses after widespread cortical ablation including bilateral removal of the occipital poles. But the latter structures are essential to the response in primates and particularly in humans. Physiologic researches of the past 15 years are helpful in reconciling these differences.

OPTOKINETIC-VESTIBULAR INTERACTION

Vestibular and visual interrelationships are particularly crucial and have been the subject of exciting experimental study in recent years. Optokinetic movements driven by rotation or "circularvection" of the entire visual environment (and thus stimulating the peripheral retina) can be used to obtain the OKN response in fishes and frogs as well as in higher vertebrates and seems more concerned with the orientation of the organism in space, that is, the coordination of the visual environment with the other highly specialized organ systems serving orientation.

I was fascinated to read of the studies of Waespe and Henn (9) in which single-unit recordings from the vestibular nucleus in alert monkeys have been obtained under controlled experimental conditions. The monkey is seated within a striped drum on a chair that will allow either rotation of the monkey, whose head is in a position to stimulate the horizontal semicircular canal or whose visual environment with optokinetic (vertical) striping may be rotated. The direction and speed of rotation of either the monkey's chair or surrounding drum may be varied independently. Thus, the visual environment can be removed by darkness or stabilized by rotating the drum and the chair at the same angular velocity, allowing independent stimulation of the labyrinth or visual fields. To summarize these investigators' findings, it can be said that when a neuron in the vestibular nucleus is found whose firing increases in response to vestibular stimulation caused by rotation in a stable visual environment (or with the eyes closed) that the same neuron will fire similarly when the visual environment is moved in a direction which simulates (by opposite motion) angular movement of the head. When the visual and rotational stimuli are applied simultaneously, as occurs in the normally functioning animal, the response is further enhanced. When the visual movement and vestibular stimulation are made to be contradictory, the signals tend to cancel and the firing rate falls off. In other words, these investigators find that any vestibular neuron that responds to vestibular stimulation by horizontal rotation will also correspondingly and appropriately react when the visual universe turns before it (circularvection) without active labyrinthine stimulation.

Evidence for this crucial interrelationship between the vestibular function and the optokinetic phenomenon in humans has accumulated over the decades. Ohm (10) described asymmetry of the optokinetic responses in a patient with vestibular imbalance. Later observers confirmed that peripheral labyrinthine input had the effect of augmenting OKN in the direction of the slow phase (OKN fast phase and spontaneous vestibular fast phase beating in the same direction). This observation was only true for peripheral vestibular disturbances. Central brainstem lesions usually depressed the optokinetic response.

Brandt et al. (11) and others studied a patient with acute unilateral labyrinthine disorder and documented the directional preponderance of a nystagmus associated with spontaneous unilateral nystagmus as well as its disappearance as the labyrinthine disturbance became quiet and/or central.
habituation occurred. Brandt et al. (11) concluded that OKN in patients suffering from primary labyrinthine lesion are not purely visually driven but must be correctly termed "vestibularly biased OKN."

**EXPERIMENTAL STUDY VERSUS OFFICE OKN**

Those of us who are office clinicians and who apply the roughshod technique of spinning the drum or moving the tape before our patients' eyes must remember that the experimental literature on OKN in humans is derived from studies of subjects surrounded entirely by a cylindrical drum with black and white stripes similar to the monkey apparatus described elsewhere (12). This arrangement is often coupled with a Barany chair that allows rotation of the patient as well as the screen in much the same way as in the study of experimental animals. Illumination, light projection, speed of the drum or chair, and intermittent sinusoidal patterns of rotation (to avoid vestibular adaptation)—all of these parameters as well as the stimulus size can be well controlled. The subject sitting in such a cylinder and observing the lateral movement of the visual environment is extremely prone to sensation of rotation of his or her own body and with this illusion is very apt to experience the quiescence and pallor and sweating that comes with vertigo—vertigo produced not by stimulation of the labyrinthine ampullae (that is, by angular acceleration of the head), but by the discrepancy of discharge of the undisturbed organ of balance in conflict with the visual illusion of rotation.

Some of you who have been in this drum have doubtlessly experienced the vertigo and nausea. But the sensation can also be created in a small movie theater such as in the Smithsonian Museum in Washington, which has steeply sloped seating and a large curved screen that wraps around the viewing horopter some 120° or more—in other words, filling the visual fields of the spectator. The museum shows a film in which the audience views a cinetape taken from the nose of an airplane whose pilot is constantly performing stunts and aerobatics. The twisting and careening environment will in short order have the spectator vertiginous, lurching about in the theater seat, and counter-rolling to compensate for the wild gyrations of the screen. This psychophysiologic observation, like the monkey experiment, demonstrates one does not need labyrinthine excitation to appreciate true vertigo; rather vertigo results from what Brandt and Daroff (13) have called the "mismatch" of sensory information between the two systems. It does not matter whether the visual or the vestibular input provides the inappropriate sensory information.

**CLINICAL APPLICATIONS**

General Comments

Once OKN begins in humans, the eyes orient themselves in a direction toward the fast phase (2). The speed of the slow phase tends to match the target speed for lower target velocities but falls off rapidly when its limit is reached.

The optokinetic component of the fast phase has been shown to have the same speed-amplitude patterns of other refixational saccades and are regarded as their equivalent. Saccadic velocity is swift and may reach speeds of 700°/s. Normally, they are capable of resetting the conjugate axes of vision with great speed and accuracy. These movements are ultimately generated by neurons within the ipsilateral pontine paramacular formation that fire in high-frequency volleys called "bursts." Simultaneously, their contralateral brain stem counterparts are actively inhibited by "pause" neurons that relax the antagonistic eye muscles.

**OKN Asymmetry in Hemispheric Lesions**

We now return to the debate that opened the clinical history of OKN—the study of cerebral disease associated with hemianopic defect and the empiric observation that when targets are taken to the side of the diseased hemisphere the optokinetic responses are diminished.

Smith, in his monograph in 1963 (14), summarized his experience with "the positive OKN sign" in homonymous hemianopic defect(s) to wit, "that it was associated with parietal lesions, especially deep ones, but not merely ones causing dense hemianopsia." To explain his findings (which were entirely with tape—drum "office" testing equipment), he favored the hypothesis proposed by Cord in 1926 (15)—that an efferent optomotor tract transversed the deep parietal lobe on its way from the visual centers to subcortical optomotor centers. An alternative explanation—the transcor-tical theory (16,26)—held that information traveling from the visual centers in the posterior hemisphere traveled forward to area eight (or frontal optomotor center), where the fast phase of nystagmus was to be initiated. This theory was attractive because the postulated insufficiency of cerebral gaze would be in the direction of the fast phase.
Historically we should mention the several fallacies that have delayed our understanding of the phenomenon. The first is that the defect was caused by a sensory (hemianopic) field loss. This proved to be untrue early in the game when Ohm (10) found dense hemianopias without the phenomenon and asymmetry was noted in patients who had rather minor visual field defects.

The second is that area eight of the frontal cortex generated the saccadic phase of OKN and that damage either to area eight or to the pathways leading to it from the occipital lobe where the perception of vision occurred (the transcortical theory) was responsible for the asymmetry. In truth, the vast majority of large frontal lesions—neoplastic, vascular, and otherwise—have not been observed to show optokinetic asymmetry. Indeed, Smith's (1) conclusion was that only in parietal lobe lesions and in large parietal lobe lesions was the asymmetry associated with hemianopsia observed.

Another indication that the fast phase of OKN was probably not at fault was that patients with optokinetic asymmetry could produce full saccades in the appropriate direction when the labyrinth was exposed to cold water stimulation. We now believe that the bulk of the fast phase comes from the brainstem neurons that generate saccades.

The most important single clue to optokinetic asymmetry in cerebral hemianopia probably was a finding that emerged in electrooculographic studies of patients with cerebral lesions.

The Clue

A hemispherectomized patient underwent total removal of the left cerebral hemisphere, diseased from birth, to control an intractable seizure disorder. Although his body was underdeveloped on the right side, he could walk and use his right hand and fingers and he also had adequate speech. But one can see an obvious optokinetic deficiency when targets are taken to the left (removed) hemisphere. Now when he is asked to pursue a visual target projected onto the screen before him, he shows on the electronic recording what we can barely and incompletely appreciate with the naked eye—a surprising abnormality in the pursuit function, which is erratic and broken up by "catch-up" saccades when targets are followed in the direction of his diseased or affected hemisphere. It would appear that his pursuit of a visual target to the left is impaired by the damage to his left hemisphere, that is, that the ipsilateral hemisphere is primarily responsible for horizontal pursuit of a moving target. This discovery offered the opportunity to support Cords' hypothesis (15) that the ipsilateral parietal lobe sent optomotor information for visual following to the brainstem in this circuit and made unnecessary and unlikely the transcortical theory and participation of the frontal cortex, which others had espoused.

In 1979, Baloh et al. (16) published a convincing study of two patients with parietal lobe lesions who had asymmetric OKN. Their studies of eye movement recordings revealed quite clearly that foveal tracking in the eyes pursuing a sinusoidally moving target was definitely erratic and disturbed when the eyes were moving toward the damaged hemisphere, an observation in keeping with previous observations of ipsilateral foveal pursuit. Full-field pursuit of a surrounding optokinetic drum was likewise impaired, but voluntary and involuntary saccades (fast components) were normal. They observed that foveal pursuit was impaired more than full-field pursuit, indicating the "active" OKN was more affected. They cited further observations indicating abnormality of the slow phase in their patients. Rotation of both patients within an optokinetic drum in light demonstrated asymmetries of the slow component in contrast to their response to rotation in dark, thus impugning the optokinetic slow-phase contribution of rotary nystagmus. The subjects were also unable to suppress vestibular nystagmus when rotary movement during visual fixation provoked slow component to the right. They concluded that a pathway running from the deep parietal lobe to the brain stem horizontal gaze center was involved, causing the asymmetry by interfering with slow-phase performance. Their observations were employed to support Cords' hypothesis (16) and Smith's (14) support of it, and to ascribe OKN asymmetry to deficit in the slow (following) phase.

It is only fair to state that optokinetic asymmetry has occasionally been reported in more frontally placed lesions (17) and that, although it is generally agreed that OKN fast phase is primarily in the brain stem, one might theorize that the frontal gaze center may be impaired by an anterior hemispheric lesion causing at least a temporary asymmetry of responses due to a "deficient saccadic" drive in the contralateral direction. This schema would be consonant with the observation that targets taken toward the damaged hemisphere produce the impaired response, in this case totally unrelated to the hemianopsia. Such asymmetries are apparently subtle and transient.

The clinical experiments designed to separate the neural pathway for foveal tracking from that
which responds to movement across the peripheral retina continue but have not yielded a definitive result. It is likely in humans that both functions utilize to some extent the same pathways, in contrast to the lower animals. It would be remembered that the hemispheric lesions in humans that cause this kind of asymmetry are not small and discrete infarcts as a general rule but either very large infarcts or infiltrative tumors that occupy a major portion of the parietal lobe. Indeed Smith (1) has always quoted Cogan as believing that in a relatively intact patient with an occipital hemianopsia, asymmetry of the optokinetic responses was a better sign of tumor than of vascular infarction.

Finally, as fate would have it, in the study of hemispheric lesions in humans, the more expensive and elaborate set-up that allows stimulation of the peripheral retina by rotation of the entire visual environment is less apt to reveal a lesion than are smaller targets on tape or drum (18). Although the latter machines cannot easily be controlled as to illumination and controlled velocity, they seem to mimic the function of foveal pursuit and stimulate the "active" OKN, which is more sensitive to a parietal lesion.

OKN Hysteria Malingering

Because OKN is an involuntary response, the automatic cooperation of the subject makes it useful in investigating visual function in animals and infants. The same property is also useful in identifying patients with hysterical visual loss or malingering, in one or both eyes; following of the tape and corrective saccades could not occur unless visual function were present.

This aspect of the test is best exploited in patients who claim severe visual loss in one or both eyes. The subject is asked to try to see what is in front of her or him and targets are moved horizontally in her or his direct line of vision. Optokinetic jerks reveal that the patient sees more than she or he claims. The patient may at times by conscious effort suppress the response, chiefly by "staring through" the close-up targets to a distant point behind them. But it is difficult to maintain this concentration. When the subject is placed within one of the rotating drums that fill the entire visual field with moving stripes, suppression of the response is practically impossible. Although a response shows that adequate vision is present to see the targets, one cannot entirely rule out the additional possibility of an organic handicap.

OKN in Disease with Loss of Saccadic Function

Marked diminution or total loss of the capacity of the eyes to make saccadic (rapid refixational) movements result in a severe visual handicap that is characteristic of a certain few diseases.

One of these is the degeneration known as "progressive supranuclear palsy," a first cousin of Parkinson's disease, in which the patient develops slow movements and dystonic rigidity of the entire body, trunk, and neck, and gradually loses all voluntary movement of the eyes, retaining only the ocular cephalic reflexes. The first eye movements to suffer are the saccades and especially in the downward direction, although all directions of gaze are affected (19). These patients often complain that they cannot see such objects as the ground beneath them, food, or the newspaper on the table before them, although it can be demonstrated that their macular vision is quite good. They become unable to move the eyes to obtain a foveal image and, for that reason, cannot examine the visual universe by moving the eyes from point to point to "regard" the environment. The lesions of this particular disorder are not in the cortex but neurons within the neural axis—in the pons, the Sylvian aqueduct, and the subthalamic areas. As in Parkinson's disease, the substantia nigra is depigmented.

This picture of saccadic paralysis may also be seen in advanced Huntington's chorea and in a variant of the Niemann-Pick neuronal storage disease called "sea blue histiocytosis" (20). Examples have been described in the hereditary disorder called "olivopontocerebellar atrophy." A rare individual is born without the ability to make saccades, a condition that Cogan has called "congenital oculomotor apraxia."

The virtue of the optokinetic test in these people is that it shows abnormalities early in the course of the disease when more casual testing of visual excursions may not reveal the diagnosis (21).

The movies demonstrate the awkward movements of the eyes, and the patient's attempt to compensate with head motion. Unfortunately, such movements of the head only lead to contraversive eye movements through the intact oculocephalic reflex. They then must hold the head still until the eyes restitute to primary position. Optokinetic testing shows only a limited slow phase tandem movement to pursue in the direction of the target but no corrective saccades (fast phase). This abnormality is found in both horizontal and vertical directions.
OKN and Internuclear Ophthalmoplegia

Early in the 1960s, Smith showed me phenomena in several patients with multiple sclerosis whose optokinetic responses showed an interesting dissociation. Targets taken to the right, for instance, provoke nystagmus in the left eye only, and vice versa. He thought this strange since the classic abduction nystagmus that would be expected in patients with multiple sclerosis showing internuclear ophthalmoplegia would be in the direction of gaze—that is, when patients are taken into right gaze, nystagmus is in the right eye only.

The finding was confirmed in several other patients, but its meaning was unclear. It was regularly associated with internuclear ophthalmoplegia, and was obvious even when internuclear ophthalmoplegia (INO) was present only to a very mild degree. As we studied this optokinetic finding further, we began to realize its value in enhancing the diagnosis of INO. The logical explanation (Fig. 1) came when we were able to examine a patient who had a unilateral INO with underaction of medial rectus on looking to the right, due to a small infarction in the floor of the fourth ventricle. Although the two bundles of the median longitudinal fasciculus lie very close together in the pontine midline at the floor of the fourth ventricle, occlusion of a small paramedian perforating artery can clearly infarct one of these and spare the other.

In examining the movies of this patient, it became clear that disassociation occurred not when gaze was evoked in the direction of targets but upon corrective saccadic return of the eyes to pick up on the oncoming stimuli. In cine sequences taken from these patients, one can clearly appreciate that the abducting eye moves over before the tardy medial rectus action of the adducting eye is brought into play.

Another dynamic maneuver in testing the eye movements helped us understand this phenomenon. Lateral gaze is usually tested with slow visual pursuit of an object held in front of the patient. But if one asked the patient with internuclear ophthalmoplegia to refixate rapidly from the primary position of gaze to a position in the lateral midfield 30°-40°, the abducting eye overshoots (dysmetria) past the target and the adducting eye demonstrates an appreciable lag (reduced saccadic velocity) in coming over to the target. We call this constellation the "ocular dysmetria sign" for INO, in which the eyes are required to make saccadic refixation to the oncoming moving targets. The adduction lag then becomes much more apparent in this test than in slow pursuit.

We then realized that OKN asymmetry was produced by the lag in the adducting eye, with excessive abduction of the abducting eye, not in the movement of pursuit (slow) phase but in the rapid (saccadic) phase of the test.

![Diagram of OKN and INO](https://via.placeholder.com/150)
These two tests then, the optokinetic test and the ocular dysmetria test (22), are both very useful in magnifying the defect of an often inapparent INO. As a matter of fact, I probably would stick with the ocular dysmetria test if I only had one to do. It will almost always bring out the defect even if it escapes detection in the casual testing of eye movements.

OKN in Retraction Nystagmus

The OKN tape or drum is also a handy device to assist in the diagnosis of lesions in the region of the cerebral aqueduct of Sylvius. Damage to the gray matter in the region of the posterior commissure and quadrigeminal plate results in a variety of abnormal neuroophthalmologic signs: pathologic lid retraction (Collier’s sign), pupillary areflexia, and paralysis of upgaze (Parinaud’s syndrome). But the most exotic manifestation in the so-called Koerber-Salus-Elschnig syndrome is the phenomenon of retraction nystagmus.

This abnormality is seen by viewing the patient from the lateral aspect to appreciate the backward jerking of the eyes with each nystagmoid beat. Although the retraction will often be provoked briefly by attempted upgaze or convergence, it is best sustained and observed by lateral inspection during testing of the vertical optokinetic responses, usually best brought out by targets down (23). When the patient is viewed from the front the nystagmus includes spasms of convergence with each beat as well as retraction movements. In this remarkable movie, one can see the patient’s eyes retracting 2-3 mm with each beat. The standard explanation is that the elevators and depressors of the eyes are firing synchronously instead of reciprocally, tugging the globe back into the orbit. This mechanism suggests a defect in reciprocal inhibition of the muscles of the IIIrd and IVth cranial nerves. Although the commonest cause of the syndrome in the middle-aged and elderly is a stroke in the high basilar distribution, this example was produced by the usual cause in the young—pineal tumor.

OKN and Congenital Nystagmus

From time to time, the ophthalmologist is asked to examine a patient with a sprained neck or headache who has been discovered to have horizontal nystagmus, often quite asymmetrical, and aggravated by lateral gaze but sometimes present even in the primary position. Those of you who are fastidious enough to do optokinetic (OKN) testing have often been in for a surprise. Instead of beating opposite to the direction of moving targets, the fast phase of nystagmus in these people will be in the same direction as the motion of the tape or drum.

Optokinetic reversal has come to be regarded as a clinical sign of specific significance although its physiology is still debated. Reversed OKN is virtually pathognomonic for congenital nystagmus. This perverse response was first demonstrated in patients who were known to show the overt familial nystagmus present from birth. Milder examples of congenital nystagmus escape detection in early life and surface later during neurologic evaluation for unrelated complaints. Most patients have a lifelong complaint of visual blurring or oscillopsia usually noted in eccentric direction of gaze.

The amplitude of the nystagmus is related to the speed of targets. When the eyes of patients with congenital nystagmus are pursuing a visual target, it has been shown that the “null point,” that eccentric attitude of gaze at which the eyes are most quiet, shifts in a direction opposite to that of the visual pursuit (24). In other words, the OKN following induces an eye position which is, in effect, strenuous lateral gaze that aggravates the fast beating nystagmus—thought by most to be a gaze modulated beating that overrides the OKN phenomenon which the examiner is trying to stimulate. The true nature of the defect in neuronal organization or structure that causes this condition is unknown.

Occasional writers have reported acquired neurologic disease can cause this reversal, but the consensus is that it is pathognomonic for congenital nystagmus (25). Studies have revealed that the wave form of congenital nystagmus during OKN stimulation are patterned exactly as those that are seen in gaze-evoked nystagmus in the same individual.

CONCLUSION

I hope that you have enjoyed this update on optokinetic nystagmus, an old and often neglected friend, whose acquaintance I made through the good offices of our celebrity, Dr. J. L. Smith. I hope that his enthusiasm is undiminished and that he will join me in urging you to apply the test appropriately in your practice, availing yourselves of its unique diagnostic benefits. This was a propitious moment to congratulate Lawton in his 60th year, half of this time having been spent in the discipline of neuro-ophthalmology. It is because of
my long friendship with him that I have written this article.

REFERENCES

Mydriasis in Giant-Cell Arteritis

James R. Coppeto, M.D., and Thomas Greco, M.D.

A previously healthy 60-year-old woman developed headache, cervical pain, bilateral mydriasis (right greater than left), and bilateral conjunctival injection as the sole manifestations of acute giant-cell arteritis.

Key Words: Mydriasis—Arteritis, giant-cell.

Mydriasis is the rarest neuro-ophthalmic association of giant-cell arteritis. Such dilated pupils are generally termed ischemic tonic pupils, principally because of pharmacologic supersensitivity, despite the fact that they are not typical tonic pupils clinically and the fact that their genesis from ischemia is purely presumptive.

We present a patient with bilateral pupillary paresis, bilateral bulbar conjunctival injection, and head and neck pain as the only manifestation of acute giant-cell arteritis. We propose that such pupils may arise from immunogenic rather than vasculogenic mechanisms.

CASE REPORT

A previously healthy 60-year-old woman experienced intermittent right periorbital headaches for 4 months followed by 1 week of right tinnitus and tenderness of the right temple and right anterior neck. She was treated with amoxicillin. Several evenings later, she noted severe bulbar conjunctival injection and a "gritty sensation in both eyes." When she woke the next morning, she found her right pupil larger than the left. She sought medical advice when she became aware of "glare" in the right eye. Her physician ordered a Westergren sedimentation rate, which was 113 mm/h. VDRL and FTA-ABS were nonreactive. Lyme enzyme-linked immunosorbent assay titers for IgG and IgM were negative (<100).

On neuro-ophthalmic consultation, the only positive findings were severe bilateral bulbar conjunctival injection and pupillary abnormalities. In ambient light, the right pupil was 7.0 mm and reacted approximately 0.3 mm to light and approximately 0.5 mm to near effort; the left pupil was 4.5 mm and reacted 0.5 mm to light and approximately 1.0 mm to near effort. A cranial computed tomographic scan and lumbar puncture as well as neurologic examination were all normal. Review of old photographs showed 3-mm pupils back to the time of her wedding pictures.
Prednisone 80 mg/day was initiated and produced almost immediate relief of all head pain. Two days later, temporal artery biopsy was performed and revealed arteritis consisting of lymphocytic and histiocytic infiltrates with multifocal destruction of the internal lamina by multinucleated giant cells.

Two days later, one drop of 0.1% pilocarpine hydrochloride in each eye produced miosis to 1 mm size of each pupil. Two months later the right pupil was 6.5 mm and reacted briskly to 5.5 mm with intense illumination or near effort. The left pupil was 4.5 mm and constricted briskly to 4 mm with intense illumination or near effort.

Thereafter, pupillary findings remained unchanged although pharmacological supersensitivity abated.

**DISCUSSION**

Davis et al. first reported mydriasis from giant-cell arteritis (1). A 69-year-old woman presented with a dilated right pupil that was fixed to light and near effort. The afferent visual system was completely spared. The pupil never recovered significant contractility and, although clinically not a tonic pupil, it was termed “tonic,” presumably solely on the basis of temporary supersensitivity to 2.5% methacholine hydrochloride. Such a designation may be inaccurate because current formulations suggest that pharmacologic pupillary supersensitivity is insufficient for diagnosis of a tonic pupil because it may occur in a variety of other innervational pupillary disorders. The case discussed by Bronster et al. (2) is virtually identical clinically and pharmacologically to that of Davis et al. except that the mydriasis was bilateral and the patient had severe bilateral permanent visual loss from ischemic optic neuropathy. The case in Currie and Lessell is significantly different from the above two cases and is somewhat unusual in its manifestations and course (3). Their patient had severe visual loss in both eyes; pupils were only mildly dilated although they showed “segmental iris contractions” and pharmacologic supersensitivity OU. However, it was interesting that the near pupillary reaction was not tonic; vision recovered significantly at 6 months in the right eye, and the right pupil recovered completely clinically although still retaining pharmacologic supersensitivity! Currie and Lessell postulate an ischemic mechanism for the pupillary abnormalities in their case.

Our patient’s findings were similar to those of Davis et al. and Bronster et al (1,2). Our patient’s temporal and cheek pain and tenderness, initially considered a manifestation of a viral illness or of migraine, were probably due to giant-cell arteritis. Her pupillary abnormalities probably reflected bilateral damage to the ciliary ganglia. Our case is distinctive because it manifested bilateral pupillary involvement without any evidence whatsoever of orbital or ocular ischemia, a manifestation difficult to reconcile with an ischemic mechanism. Barricks et al. reported a case that in many ways is the converse of our case (4). Their patient had total ophthalmoplegia from massive, necrotizing, orbital giant-cell arteritis, yet had total sparing of the ciliary ganglia histopathologically and appeared to have relatively normal pupillary functioning, considering the severe degree of visual loss. In their case the ciliary ganglia appeared to be a relatively “privileged” site with regard to orbital ischemia. Moreover, mydriasis appears to be relatively uncommon even in clearly documented ophthalmoplegic cases of giant-cell arteritis, with miosis actually being the rule rather than mydriasis (5).

The bilaterality of the findings in our patient without any evidence of ocular ischemia as well as the lack of evidence of mydriasis in cases of ophthalmoplegia in giant-cell arteritis have led us to suspect that the etiology of the mydriasis that rarely occurs in giant-cell arteritis may be an immunological attack on the parasympathetic pupillary innervation, somewhat analogous to cases of mydriasis associated with infections and some autonomic neuropathies. Immunologic abnormalities occur in giant-cell arteritis. These include the variable presence of anti-nuclear antibodies, the occasional deposition of IgM and IgG on arterial basement membrane (6), the presence of both T4 helper/inducer and T8 cytotoxic/suppressor lymphocytes (6), the frequent elevation of C-reactive protein (7), elevated levels of circulating immune complexes (8) (by Raji cell radioimmunoassay), and the association of HLA-DR antigens (9).

The clinical correlates of such abnormalities may include peripheral neuropathy, microangiopathic hemolytic anemia, pernicious anemia, synovitis, and uveitic glaucoma (10-12). In this regard we have described a case of bilateral uveitic glaucoma in a patient with giant-cell arteritis without ischemic optic neuropathy in which the mechanism of the uveitis appeared to be at least partially immunologic and not solely ischemic (12).

In conclusion, mydriasis is an exceedingly rare accomplishment of giant-cell arteritis. Such cases have not been documented to evolve into tonic pupils, although pharmacologic supersensitivity is uniformly present and in one instance, some aspects of a clinical tonic pupil were transiently
present. There is no proof that such pupillary abnormalities are ischemic in origin. It is equally likely that they represent a manifestation of one of the rare immunological disturbances in giant-cell arteritis.

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REFERENCES

Bilateral Central Retinal Artery Occlusion in Occult Temporal Arteritis


A rare case of bilateral central retinal artery occlusion due to occult temporal arteritis is reported. We stress temporal artery biopsy in every patient with central retinal artery occlusion in old age.

Key Words: Central retinal artery occlusion—Temporal arteritis.

Bilateral central retinal artery occlusion is extremely uncommon and accounts for only 4–7% of all central retinal artery occlusions (1,2). Although temporal arteritis is responsible for only 3–10% of central retinal artery occlusions (1–3), most of the bilateral central retinal artery occlusions in elderly patients are due to temporal arteritis (1,4,5). To prevent central retinal artery occlusion in the other eye, a strong suspicion of temporal arteritis must exist.

CASE REPORT

A 65-year-old man presented to us with sudden loss of vision in the right eye for 2 days, unaccompanied by any significant systemic complaints. On examination, his visual acuity was counting fingers in temporal quadrant in the right eye and left eye vision was 6/12. The intraocular pressure was normal and the anterior segment was unremarkable in both eyes. Ophthalmoscopy of the right eye revealed narrowed retinal arteries, marked opacification of the posterior pole, and a cherry-red spot suggestive of central retinal artery occlusion. A triangular area of retina between the macula and optic disk supplied by a cilioretinal artery was normal (Fig. 1, top). Three days later, he reported sudden loss of vision in his left eye preceded by several transient obscurations of vision and was seen in the emergency service after ~7 h. At that time, he had a visual acuity of counting fingers at 1 m in his left eye. Ophthalmoscopy of this eye revealed a picture of central retinal artery occlusion with narrowed retinal arteries, cattle-trucking, opacification of the posterior pole, and a cherry-red spot. There was no cilioretinal artery in this eye. Within eight hours, visual acuity in this eye dropped to perception of light and ophthalmoscopy showed further opacification of the retina (Fig. 1, bottom).
FIG. 1. Top: Central retinal artery occlusion and a triangular area of normal retina supplied by a cilioretinal artery in the right eye. Bottom: Central retinal artery occlusion in the left eye.

Both eyes were treated with immediate paracentesis and retrobulbar injection of Duvadilan (isosuxprine hydrochloride) 10 mg but this did not improve his vision. On investigation, his blood pressure, blood sugar, total and differential leukocyte count, lipid profile, coagulogram, cardiac status, and blood flow in both the carotid arteries on Doppler scan were normal. The erythrocyte sedimental rate done twice was 12 and 10 mm in the 1st hour by the Westergren method. Results of tests for rheumatoid factor, lupus erythematosus, and VDRL were negative. A chest x-ray film showed unfolding of aorta and an x-ray film of the cervical region showed no calcification in the carotid arteries. Temporal arteries on both sides were palpable, nontender, and pulsatile. Biopsy of the left temporal artery showed an organizing thrombus, focal infiltration of the adventitia and intima by lymphocytes, histiocytes and eosinophils, and fragmentation of the internal elastic lamina diagnostic of temporal arteritis (Fig. 2). Giant cells were not present. A 60-mg prednisolone tablet once a day was instituted only after the temporal artery biopsy report became available. His vision in the left eye improved to counting fingers close to the face after 2 weeks of systemic corticosteroids, and showed no further improvement. Vision in the right eye did not improve and subsequently he developed optic atrophy and macular degeneration in both eyes.

DISCUSSION

In temporal arteritis, one eye is usually affected first and the other eye is involved after an interval of days or weeks. In view of a higher incidence of
unilateral or bilateral irreversible visual loss in untreated cases and the demonstrated protective action of high-dose corticosteroids, an early diagnosis and prompt treatment of this disorder is of prime importance. In classic temporal arteritis, the presence of signs in the temple, general symptoms, and a raised sedimentation rate help in the diagnosis. However, the occult form of the disease is more common than the classic variety (5), and in the former classic symptoms and the temporal artery signs are usually absent but a raised sedimentation rate is a good guide to the diagnosis although not absolute. Isolated cases of normal sedimentation rate in temporal arteritis have been reported (3,6,7), although in larger series the incidence of normal sedimentation rate may be as high as 8–10% (8; J. Smith, unpublished data, 1989). Our patient belongs to the category of occult temporal arteritis. He had no temporal artery signs and symptoms with a persistently normal sedimentation rate, which misled us, and the diagnosis was delayed. This case amply illustrates that in unilateral or bilateral central retinal artery occlusion in the elderly, the possibility of temporal arteritis cannot be ruled out and a temporal artery biopsy should become a part of the routine workup even if the sedimentation rate is normal.

REFERENCES
Pseudodrusen of the Optic Disc

Papilledema Simulating Buried Drusen of the Optic Nerve Head

John E. Carter, M.D., Michael D. Merren, M.D., and Barry M. Byrne

The distinction between true papilledema and pseudopapilledema rests on characteristics of the optic disc when examined ophthalmoscopically. Buried disc drusen frequently simulate papilledema and often result in misdirected diagnostic maneuvers in search of a cause for presumed intracranial hypertension. When an elevated optic disc exhibits an irregular, "lumpy, bumpy" border, a diagnosis of buried drusen of the optic nerve is usually made. We report a case with papilledema secondary to increased intracranial pressure in which the margins of the swollen optic disc presented this lumpy, bumpy border characteristic of buried drusen. The lumpy character of the disc border disappeared with resolution of the papilledema, and ultrasonography demonstrated the absence of any buried drusen. Other characteristics of papilledema, including extension of the disc swelling into the peripapillary nerve fiber layer, telangiectasia of the superficial vessels of the optic disc, and obscuration of the retinal vessels as they crossed the margins of the optic disc, provided strong evidence of true papilledema and remain the most reliable findings allowing a distinction between true papilledema and pseudopapilledema.

Key Words: Papilledema—Drusen—Optic nerve.

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had a "lumpy, bumpy" outline strongly indicative of optic nerve drusen, but there was also swelling present in the peripapillary nerve fiber layer with obscuration of the retinal vessels as they crossed the optic disc onto the retina and mild telangiectasia of the superficial vessels of the optic disc. There was no indication of drusen on the left side, which did exhibit mild but definite papilledema. The results of a computed tomographic examination with and without contrast were normal except for minimal effacement of the right lateral recess of the fourth ventricle. The lateral and third and fourth ventricles were not dilated. Magnetic resonance imaging (MRI) (Fig. 2) demonstrated a process fusely enlarging the right cerebellar hemisphere and involving primarily the cerebellar cortex, impinging on the cerebellar white matter. A gyriform pattern was seen that corresponded to the enlarged but preserved folia of the cerebellar cortex. Exploration and decompression of the posterior fossa were achieved by amputation of the lateral one-third of the right cerebellum. Pathologic study of the involved cerebellar cortex confirmed the diagnosis of dysplastic gangliocytoma of the cerebellum (Lhermitte-Duclos disease).

Following surgery, the patient made an uneventful recovery. No residual neurological deficits were present except for continued mild hypo-
PSEUDODRUSEN OF THE OPTIC DISC

FIG. 2. Magnetic resonance image of the posterior fossa showing abnormal signal intensity of the right cerebellum. The abnormality has a gyriform appearance characteristic of the pathologic picture of dysplastic gangliocytoma of the cerebellum, which the lesion proved to be at surgery. Reproduced with permission from Carter et al., J Neurosurg 1988;00.

FIG. 3. Orbital echography of the right eye 3 months after posterior fossa decompression. Vertical axial scan at normal amplification (a) and horizontal axial scan at low amplification (b) indicate that the optic nerve is still slightly elevated by echography. However, the high reflectance pattern characteristic of buried drusen of the optic nerve is not present.

FIG. 4. Ultrasound B-mode scan echogram in a patient with drusen of the optic nerve head for comparison with the patient presented here. With low amplification the surface of the optic nerve head exhibits a high reflectance abnormality representing drusen.

tonia on the right side and no neurological symptoms have occurred during a 6-month follow-up. The papilledema underwent gradual resolution (Fig. 1c and d). As the disc edema in the right eye resolved, the optic disc became clearly visible and the irregular border of the swollen disc resolved into an entirely normal optic nerve with no evidence of visible or buried drusen. An echographic study (Fig. 3) confirmed the absence of any drusen bodies in the optic nerve.

DISCUSSION

The subject of this report presented with vague, lateralized headache and visual symptoms attributable to papilledema, but also seen in conditions with full optic discs including optic disc drusen and optic disc dysplasias (1). The most dramatically elevated optic disc showed a markedly irregular border that strongly suggested the presence of buried drusen. There were even one or two very small, bright refractile areas in the superficial disc substance. Despite this irregular border, there was blurring of the peripapillary nerve fiber layer, obscuration of the retinal vessels as they crossed the disc margins, and telangiectasia of several superficial disc vessels, enabling a firm diagnosis of papilledema in this eye, which was confirmed by the mild papilledema with no signs of drusen in the fellow eye. The lumpy appearance of the optic disc was so dramatic, however, that the diagnosis was presumed to be true papilledema superimposed on buried disc drusen.

A diagnosis of buried drusen might have delayed the diagnosis of intracranial hypertension secondary to a cerebellar mass lesion, especially if MRI had not been available to demonstrate the striking abnormality in the patient’s cerebellum. Chronic papilledema is well known to produce visible intrapapillary refractile bodies in the superfi-
cial nerve fiber layer that have been reported to result in the misdiagnosis of optic disc drusen and delay the diagnosis of intracranial hypertension (11). These small refractile bodies are now widely recognized as a consequence of chronic disc swelling (4,5,7,8,10,11) and should not be mistaken for drusen of the optic nerve head. However, no case has been reported in which buried drusen of the optic nerve have been mimicked in the fashion demonstrated in this patient.

In their textbooks, both Glaser (1) and Miller (4) enumerate criteria for distinguishing pseudopapilledema from true papilledema. While a lumpy, bumpy border to the optic disc is very suggestive of optic disc drusen, specific characteristics of the optic disc swelling, including edema of the peripapillary nerve fiber layer, telangiectasia of the superficial vessels of the optic nerve head, and obscuration of the retinal vessels as they cross the optic disc, should be used to distinguish true papilledema from pseudopapilledema.

REFERENCES

Optic Neuropathy in Behçet’s Disease

Tulay Kansu, M.D., Pinar Kirkali, M.D., Emin Kansu, M.D., and Turgut Zileli, M.D.

Optic neuropathy in Behçet’s disease is rare, despite wide ocular and neurological involvement. Progressive atrophy of the optic disc and severe visual loss is not uncommon in Behçet’s disease; however, visual loss due to acute optic neuropathy is less well known. We report three cases of optic neuropathy in Behçet’s disease. The clinical picture was variable in our patients, presenting either as acute retrobulbar optic neuritis or anterior optic neuropathy. It is interesting to note that although the neurological picture resembles multiple sclerosis, there seems to be less predilection to optic nerve involvement in Behçet’s disease.

Key Words: Behçet’s disease—Optic neuropathy.

CASE REPORTS

Patients were drawn from the records of the Behçet’s disease clinic of the Hacettepe University Hospitals. Two hundred patients had registered over a period of 8 years, and 65 of them had neurological manifestations. Optic neuropathy was found in only three patients. The diagnosis of Behçet’s disease was made when two of three major criteria were present (oral and/or genital ulcers and eye involvement) and minor features were apparent (skin, joint, vascular, and nervous system manifestations). Patients with optic atrophy who had active inflammation or papilledema prior to the detection of optic neuropathy were not included.

Case 1

A 32-year-old man presented in November, 1982, complaining of acute loss of vision in his left eye. He had a history of recurrent oral and genital ulcers, arthralgia, and thrombophlebitis during the past 4 years; no diagnosis had been made.

On examination, visual acuity (VA) was 20/20 OD and only light perception OS. There was an
afferent pupillary defect in the left eye. The vitreous was clear in slit lamp examination. Ophthalmoscopic examination revealed normal findings in the right eye. In the left eye the optic disc was pale, the macula was edematous, surrounded with small exudates, and sheathing was observed in retinal veins.

Three months later, he developed visual blurring in the right eye. VA was 20/100 OD and light perception OS. A central scotoma in the right eye was detected with confrontation and Amsler Grid cards. Ophthalmoscopic examination revealed optic disc edema with peripapillary exudates and hemorrhages OD and optic atrophy OS. Serum VDRL was negative. Lumbar puncture (LP) pressure was normal, and protein was elevated (55 mg%) in cerebrospinal fluid (CSF). No cells were detected under microscopic examination.

A diagnosis of Behçet's disease was made on the basis of clinical findings; the treatment with prednisolone 60 mg daily and cyclophosphamide 50 mg twice daily was started. One month later the right disc was pale, and VA was 20/50 in the right eye. No follow-up examination was available until 4 years later when he presented with abdominal pain, which was thought to be related to a peptic ulcer. He had no further visual complications but had recurrent aphthous lesions in the mouth. VA was 20/30 OD and hand motion OS.

Comments

This patient had findings of a pale disc and retinitis OS and papillitis OD 3 months apart without active inflammation in the eye. His past history and elevated protein in the CSF was compatible with Behçet's disease.

Case 2

A 25-year-old man was first seen in September, 1980, with right peripheral facial palsy, bilateral abducens nerve paresis, and swollen optic discs. VA was 20/40 OD and 20/70 OS. There was a para-central scotoma in the right eye and a small central scotoma on the left on perimetric examination.

Computerized tomography of the brain was normal. LP pressure was 170 mm H₂O, and there were only 2 mononuclear cells. Serum VDRL was negative. He recovered completely 1 month later. He was thought to have multiple sclerosis (MS) with bilateral optic neuritis.

In April, 1981, he was admitted again with blurred vision, gait disturbance, and urinary hesitancy. Physical examination disclosed oral aphthae and a scar of scrotal ulceration. He was ataxic. There was a right sixth nerve palsy, and deep tendon reflexes were increased. Bilateral plantar reflexes were extensor. He was clumsy in cerebellar tests. VA was 20/70 OD and 20/70 OS. Visual field examination was similar to the previous fields. In the color vision test he was able to read only 5 of 12 Ishihara plates OU. Optic discs were pale bilaterally. There were no signs of ocular inflammation. Behçet's disease was considered as a diagnosis, and corticosteroid treatment was given. Visual symptoms remained unchanged, but cerebellar findings improved slightly.

In December, 1981, he was seen again because of a generalized convulsion. He was stable until 1983, when he developed blurred vision in the left eye. On examination he had aphthous lesions in the mouth and papular lesions on the scrotum. VA was 20/40 OD and 20/200 OS. Slit lamp examination revealed cells in the vitreous, posterior synechiae, and uveal pigmentation in the lens of the OS. Optic discs were both pale, suggesting atrophy. Phenytoin and cyclophosphamide were added to the treatment, along with the topical treatment for uveitis. His vision returned to a 20/70 level after the inflammation subsided.

Comments

This patient had optic disc edema with decreased vision and normal LP pressure. He was thought to have bilateral optic neuritis with simultaneous onset, resulting in atrophy. He developed uveitis 3 years later, completing the three major criteria for the diagnosis of Behçet's disease.

Case 3

A 22-year-old woman was first seen in April, 1977, with acute visual loss in the right eye. VA was 20/70 OD and 20/20 OS. There was a central scotoma in the right eye. Ophthalmoscopic examination was normal. Retrobulbar neuritis was considered, and she was given oral corticosteroids. One month later her vision recovered completely.

She was seen again 2½ months later because of paresthesias in her feet, but her neurological examination was normal. In March, 1978, she was seen again because of visual loss in the left eye. The diagnosis of retrobulbar neuritis was made by the ophthalmology department, but details of her eye examination were not available. On physical examination, she had oral aphthous lesions and genital ulcerations in the labia major. She was thought to have Behçet's disease. Prednisolone
DISCUSSION

Behçet’s disease is characterized by three primary components: iridocyclitis (historically with hypopyon), aphthous lesions in the mouth, and ulceration of the genitalia. Erythema nodosum, arthropathy, and thrombophlebitis often accompany these manifestations. The etiology and pathogenesis of Behçet’s disease is not well understood, although immunologic mechanisms have been suspected to be pathologically important because of its vasculitic nature and the cellular characteristics (2). Involvement of the central nervous system occurs in approximately 10% of patients, and the frequency of ocular manifestations in Behçet’s disease is between 70 and 85% (2). The underlying disease in all organ systems is an occlusive vasculitis, and the most common ocular finding is anterior uveitis (iritocyclitis). Posterior segment manifestations include localized retinal edema, macular edema, perivascular sheathing, and occlusion of retinal vessels. The presence of necrotizing retinal vascular lesions is well known and is often obscured by the severity of the anterior reaction. Optic nerve damage can follow the extension of an inflammation from the uvea to the mesenchymal tissue surrounding the nerve fibers (uveopapillitis). Papilledema in the absence of uveitis is also a well-recognized feature of the disease as a manifestation of benign intracranial hypertension (3). In our experience such cases are seen more often than are cited in the literature. Of our 65 patients with Behçet’s disease and neurological manifestations, 20 had benign intracranial hypertension (unpublished data).

However, optic nerve disease without intracocular inflammation or papilledema is rare. There is only one well-documented report of optic neuropathy in Behçet’s disease (4). Scouras and Koutroumanos (4) described typical anterior ischemic optic neuropathy in two patients with Behçet’s disease, presumably on the basis of posterior ciliary arteritis. Cotticelli et al. reported an unusual case of Behçet’s disease with bilateral obliterating retinal panarteritis and ischemic optic atrophy (5).

Colvart et al. (6) reviewed the ocular manifestations of Behçet’s disease in 32 patients. Inflammatory involvement of the optic nerve in the form of papillitis is reported in three patients; however, no details of the optic nerve process were given.

In another review, Atmaca (7) reported edema in 51 and atrophy in 17 eyes of a total 148 eyes of 83 patients with Behçet’s disease, but the clinical details were scanty, and the possibility of optic atrophy due to severe retinal vascular disease was not addressed.

Histopathological studies of the optic nerve and retina based on three cases have shown that changes in the optic nerve developed secondary to principal changes in the retina in two cases (8). Findings in the third case showed that such changes may start primarily in the optic nerve, manifested by fibrous astrocyte substitution for the axonal portion of the optic nerve. The capillary network was still intact despite extensive narrowing of the central retinal artery (8).

Syphilis was considered in the differential diagnosis of our patients. Serum VDRL was negative in patients 1 and 2 and not done in patient 3. The incidence of syphilis is very low in Turkey, and the fluorescent treponema antibody absorption (FTA-ABS) test is not available. Treponema pallidum immobilization (TPI) is done if the suspicion is high. Our clinical impression was that these patients did not have syphilis, although we do not have definitive serological proof.

The similarity of the clinical picture in multiple sclerosis and Behçet’s disease is well known. Clinical comparative studies for these two diseases showed a very low incidence of optic nerve involvement in Behçet’s disease, in spite of a high incidence of visual impairment due to optic neuritis in multiple sclerosis (9).

Our cases as well as those in the literature suggest that optic neuropathy in Behçet’s disease can be caused by (a) ischemic process (4), (b) demyelination (2), (c) inflammation (6), or (d) secondary invasion of the optic nerve from the processes that have involved the uvea and retina (8).

We believe that the pathogenesis is occlusion of the small vessels of the optic nerves and demyelination on the basis of mild ischemia. Axonal damage and necrosis occur in more severe cases.

In conclusion, we have reported data from three cases of optic neuropathy in Behçet’s disease. The optic nerve appears to be less involved. While not common, optic neuropathy in Behçet’s disease can
present as retrobulbar neuritis or anterior optic neuropathy.

REFERENCES

Blepharospasm Associated with Olivopontocerebellar Atrophy

Abdorasool Janati, M.D., W. Steven Metzer, M.D., Robert L. Archer, M.D., Jess Nickols, M.D., and Jugalkishor Raval, M.D.

We report two cases of cranial dystonia (blepharospasm) associated with olivopontocerebellar atrophy (OPCA). The pathophysiology of blepharospasm appears to involve an increased excitability of the interneurons of the blink and corneal reflexes. It is hypothesized that blepharospasm associated with OPCA might be due to rostral brainstem lesions disrupting central dopaminergic and cholinergic pathways, resulting in disinhibition of brainstem reflexes or denervation supersensitivity of the facial nuclear complex.

Key Words: Blepharospasm—Meige's syndrome—Dystonia—Movement disorders—Olivopontocerebellar atrophy—Cerebellar degeneration.

Olivopontocerebellar atrophy (OPCA) was described by Dejerine and Thomas in 1900, who distinguished the entity from Friedreich's ataxia and the "hereditary cerebellar ataxia" of Marie, while noting a similarity to the familial ataxia reported by Menzel in 1891 (1). Until recently, OPCA has been considered a rare pathological entity, with only 117 anatomically confirmed cases reported until 1980 (2). Many now consider OPCA to be a clinical syndrome comprising a large heterogenous group of disorders that share clinical features of the hereditary ataxias, parkinsonism, and the hereditary choreas. Some cases are dominantly or recessively inherited, whereas others appear to be sporadic (1). There is controversy regarding the utility of this concept of such a heterogenous clinical entity as OPCA, with some arguing that cases of OPCA should simply be considered variants of multiple system degeneration (3).

Blepharospasm is a relatively uncommon condition that has been estimated to have a prevalence of 1 in 10,000. Onset is usually between the ages of 50 and 70 years, and women are more commonly afflicted than men. Only occasionally is there a family history of the disorder (4). Blepharospasm consists of repeated, involuntary, bilateral contractions of the orbicularis oculi muscles. It often begins as an increase in the spontaneous blink rate and may gradually progress to occupational and social disability and functional blindness (4–6).

Idiopathic blepharospasm alone is commonly referred to as essential blepharospasm. Idiopathic blepharospasm combined with orofacial dystonia has been referred to as orofacial–cervical dystonia, blepharospasm–oromandibular dystonia syndrome, Meige's syndrome, and Brueghel's syndrome. Some consider blepharospasm alone or oromandibular dystonia alone to be formes frustes...
of the complete syndrome (4). It is commonly accepted that the syndrome was first described by Henry Meige, a French neurologist, in 1910, who termed it “spasme facial median,” although Marsden has pointed out that the syndrome was recognized by Pieter Brueghel, the Elder in the 16th century (7).

We report two cases of OPCA, one sporadic and one familial, associated with blepharospasm and orofacial dystonia.

CASE REPORTS

Case 1

A 56-year-old man noted the onset, at age 44, of unsteadiness, gait disturbance, slurred speech, dysphagia, and urinary incontinence. These symptoms insidiously progressed, and he became wheelchair bound at age 53. The onset of involuntary blinking and facial movements was noted about that time. Neurological evaluation at another institution included computed tomography (CT) of the head, which revealed cerebellar and pontine atrophy. A diagnosis of OPCA was made. Further evaluation at age 54 years included electrodiagnostic testing, which indicated a sensorimotor axonopathy. Laboratory studies included hemogram, serum electrolytes, calcium, blood urea nitrogen, creatine, T4, and arterial blood gases, which were unremarkable. The symptoms noted continued to progress insidiously. No change in mentation occurred. There is no history of exposure to dopaminergic receptor-blocking drugs until age 56, when metoclopramide was prescribed for a few weeks for dyspepsia. There was no family history of any neurological disorders. He was readmitted at age 56.

General physical examination revealed a well-nourished white man who was wheelchair bound, and was otherwise unremarkable. Neurological examination revealed normal mental status. Speech was scanning and dysarthric. Cranial nerves were intact. There was no evidence of a Kayser-Fleischer ring. Optokinetic nystagmus was intact. Ocular dysmetria and hypometric saccades were evident. Frequent involuntary contraction of the orbicularis oculi muscles was noted, with a blink rate of 40/min. Involuntary orofacial dystonic movements were present. Bilateral intention tremor and dysmetria were present with attempted trajectory movements of the upper extremities. Severe truncal ataxia prevented standing without assistance. Mild distal muscular atrophy and weakness were present, with minimal diffuse rigidity. Myotatic reflexes were slightly, diffusely hyperactive, and plantar reflexes were extensor bilaterally. A repeat head CT scan demonstrated severe cerebellar and pontine atrophy (Fig. 1).

Case 2

A 52-year-old woman noted the onset of gait disturbance and lower extremity weakness in her 20s, which progressed insidiously. At about age 45, she noted the insidious onset of slurred speech, and she began to experience involuntary, forceful eye closure at about age 49, particularly in response to bright light. Five of her seven siblings were similarly afflicted, but with no history of involuntary eye closure. No change in mentation was noted, and there was no history of exposure to dopaminergic receptor-blocking drugs.

General physical examination was unremarkable. A neurological examination revealed normal mental status. Scanning, dysarthric speech was present. Cranial nerves were intact. There was no evidence of a Kayser-Fleischer ring. Frequent involuntary contraction of the orbicularis oculi muscles was noted. Involuntary orofacial dystonia was present. Trajectory movements of the upper extremities were normal, but severe lower extremity and truncal ataxia was present. Myotatic reflexes were slightly, diffusely hyperactive, and plantar reflexes were extensor bilaterally. Nerve conduction testing and head CT were normal.

FIG. 1. Computed tomography of the head in case 1 demonstrates severe cerebellar and pontine atrophy.
DISCUSSION

Clinical features reportedly associated with OPCA are diverse. Duvoisin considers cerebellar dysfunction and extrapyramidal dysfunction to be essential features. Other features often present include corticospinal tract manifestations and cerebellar eye signs. Features of variable occurrence include supranuclear ophthalmoplegia, optic nerve atrophy, retinal degeneration, orthostatic hypotension, incontinence, impotence, anhidrosis, myoclonus, amyotrophy, and dementia (1). Extrapyramidal dysfunction is most commonly manifest as bradykinesia and rigidity, with these parkinsonian features being present in most patients. Generalized and focal dystonias have been recognized, with torticollis probably being the most common focal dystonia associated with OPCA (2,8-10).

Ocular dysfunction reported in OPCA has included nystagmus, jerky pursuit, fixation instability, ocular dysmetria, hypometric saccades, loss of optokinetic nystagmus, slowing of saccades, and supranuclear ophthalmoplegia (1). We are aware of only four previously reported cases of blepharospasm associated with OPCA (11-15).

OPCA has been characterized pathologically by atrophy due to neuronal loss in the cerebellar cortex, basis pontis, and inferior olivary nuclei. There also may be neuronal loss in the spinal cord, cerebral cortex, and basal ganglia (16). Anatomical pathological studies of the brainstem of OPCA patients have revealed gliosis or neuronal loss of the arcuate, pontine, inferior olivary and pontobulbar nuclei.

Purkinje cell loss reportedly results from an anterograde transsynaptic degenerative phenomenon. Atrophy or gliosis has been reported to involve multiple areas of the reticular formation. The central tegmental fasciculus and various cranial nerve nuclei have also been involved in various cases (2). Neurophysiological investigations have frequently detected abnormal brainstem auditory evoked potential latencies in patients with OPCA (1).

Phenomenologically, blepharospasm is considered to be a focal dystonia (4,7,11,15). Electromyographic recording of facial muscles with blepharospasm indicates irregular bursts of cocontraction activity in these muscles lasting 200-300 ms to many seconds. These burst durations are much longer than those seen with myoclonus, tics, and chorea; they resemble spasms seen with generalized torsion dystonia (17). Blepharospasm is commonly accompanied by oromandibular dystonias and sometimes by spasmodic dysphonia or axial dystonia, such as torticollis (7,11).

A detailed electrophysiological study found a number of abnormalities in patients with blepharospasm. Electromyographic activity was noted to be similar to that seen in other dystonic muscles. Amplitude and duration of the R1 and R2 components of the blink reflex were both increased, and some patients exhibited R1 on the side contralateral to the stimulus. The excitability cycle of recovery of the blink reflex was enhanced. Unlike voluntary blinking, electroencephalographic backaveraging failed to reveal any Bereitschafts potential (readiness potential) preceding blepharospasm. These collective observations have led to the conclusion that there is an increased excitability of the interneurons of the blink and corneal reflexes with blepharospasm, and that this is probably due to drive from pathways from the basal ganglia (17).

There have been few pathological studies of idopathic blepharospasm. One recent postmortem examination of a patient with Meige’s syndrome revealed neuronal loss in the substantia nigra, locus ceruleus, midbrain tectum and dentate nuclei, as well as Lewy bodies in the brainstem pigmented nuclei (18). Another recent pathological investigation found a small angiomia in the dorsal pons at the site of the central tegmental tract in a patient who had been diagnosed as having essential blepharospasm. In three other cases of idiopathic cranial dystonia, no significant brainstem abnormalities were detected (19). Blepharospasm clinically similar to essential blepharospasm has been reported in patients with multiple sclerosis plaques of the rostral brainstem, and with infarctions of rostral brainstem nuclei, bilaterally (12,14,20-22). Neurophysiological and pathological findings thus provide some evidence of brainstem pathology or enhancement of basal ganglia brainstem “drive” playing a role in the genesis of blepharospasm.

Delayed onset of dystonia in a patient with static encephalopathy has been attributed to “sprouting” of surviving neurons (23). Similarly, disruption of central dopaminergic and cholinergic pathways due to rostral brainstem lesions, as seen with OPCA, might result in disinhibition of brainstem reflexes or denervation supersensitivity of the facial nuclear complex, resulting in cranial dystonia, such as blepharospasm (12,13,24). This pathophysiological model is supported by the observation that another movement disorder, palatal myoclonus, possibly results from delayed denervation supersensitivity after a lesion of the inferior olive (25). Interestingly, a case of blepharospasm
associated with palatal myoclonus has been reported (13).

REFERENCES

Isolated, Pupil-Sparing Third Nerve Palsy as Initial Manifestation of Systemic Lupus Erythematosus

Elliot D. Rosenstein, M.D., Joseph Sobelman, M.D., and Neil Kramer, M.D.

A 29-year-old woman had an isolated, pupil-sparing third cranial nerve palsy. Serologic and CSF abnormalities and the subsequent course were consistent with systemic lupus erythematosus. Corticosteroid therapy resulted in improvement of ocular palsy within 4 weeks. The pathogenesis of cranial neuropathy in systemic lupus erythematosus and the unique presentation in this patient are discussed.

Key Words: Systemic lupus erythematosus—Cranial neuropathy—Oculomotor nerve.
full. Ptosis was present on the left. The left eye was deviated outward and slightly depressed. There was inability to move the eye upward or downward. There was no nystagmus, and ocular motility was full in the right eye. The remainder of the neurologic and general physical examination was normal. There was no improvement in ocular motility after administration of edrophonium chloride.

Computed tomography of the head and orbits, with and without contrast, and cerebral angiography were normal. Cerebral spinal fluid analysis revealed protein 76 mg/dl (normal, 14-45 mg/dl) and slight lymphocytosis, 12 cells/mm³; oligoclonal bands were absent. Erythrocyte sedimentation rate was 63 mm/h (Westergren). Complete blood count, 4-h glucose tolerance, and thyroid function tests were normal. Serologic testing for syphilis [rapid plasma reagin (RPR)] and Lyme disease [enzyme-linked immunosorbent assay (ELISA)] were negative. LE prep was positive. Anti-nuclear antibody was positive at titer 1:2,560, homogenous pattern; antibodies to DNA, RNP, Smith, SS-A (Ro), and SS-B (La) were absent. Anti-cardiolipin antibody determination was not done. The level of C3 was 65 mg/dl (normal, 84-140 mg/dl), C4 was 12 mg/dl (normal 18-45 mg/dl).

Prednisone, 1 mg/kg, was administered with improvement of gaze palsy within 3-4 weeks. During the following 4 months, her regimen was reduced to alternate day corticosteroids and eventually discontinued.

During the next 8-12 months, she subsequently noted the onset of periods of morning stiffness with painful swelling of her digits; cold- and emotion-induced Raynaud's phenomenon of her fingers; pleuritic chest pain without documented effusion—all of which have been treated with nonsteroidal medications and supportive measures. Renal function and urinalysis remained normal. There has been no recurrence of her ocular palsy or development of other neurologic findings.

**DISCUSSION**

Isolated pupil-sparing third nerve palsies in adults are most often caused by microvascular infarction (6). In the patient presented here, there was no identifiable vasculopathic risk factor other than the history of smoking. The presence of tumor or aneurysm was excluded by the radiographic procedures. Systemic lupus erythematosus seemed the most plausible explanation for her presentation.

Neuro-ophthalmologic manifestations of lupus are diverse and include disorders of the orbits, visual system, and oculomotor pathways. These abnormalities are listed in Table 1, based on anatomic localization.

We are aware of only one prior report of ocular palsy as the sole initial clinical manifestation of lupus. Sedwick and Burde (18) reported a young women with an isolated sixth nerve palsy who additionally had leukopenia and positive fluorescent antinuclear antibody, consistent with lupus. Her symptoms improved without treatment, and she subsequently showed no further evidence of active lupus.

Third nerve palsy has been noted in only a few previous reports (5,19,20). The best substantiated case was reported by Johnson and Richardson (5) (case 3), who noted a transient, pupil-sparing, third nerve palsy in a patient with multisystem involvement due to lupus. Death was attributed to renal failure 7 years later, and postmortem examination revealed a totally normal brainstem. The peripheral portion of the cranial nerve was not examined.

Isolated, nontraumatic, third nerve palsy, sparing the pupil, has traditionally been ascribed to microinfarction due to diabetes, hypertension, or atherosclerosis. The classic oculomotor lesion, as seen in diabetes, involves the nerve at the brainstem level in its subarachnoid and cavernous portion. Asbury et al. (21) found hyalinization and endothelial proliferation resulting in luminal narrowing in some of these vessels. Due to involvement of the vasa nervorum, central axons and myelin sheaths were destroyed. The nerve periphery, where the pupillary-motor fibers dominate and which receives its blood supply from the arachnoidal vessels, was spared.

**TABLE 1. Neuro-ophthalmologic manifestations of systemic lupus erythematosus**

<table>
<thead>
<tr>
<th>Orbital lesions</th>
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<tr>
<td>Orbital pseudotumor (7)</td>
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<td>Tolosa-Hunt syndrome (8)</td>
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<th>Anterior visual pathway</th>
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<tr>
<td>Papilledema (3)</td>
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<tr>
<td>Pseudotumor cerebri (10,11)</td>
</tr>
<tr>
<td>Optic neuropathy (12)</td>
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<td>Retinal vascular disease (13)</td>
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<th>Retrochiasmatic pathway</th>
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<tr>
<td>Visual field defects (14)</td>
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<tr>
<td>Cerebral blindness (14)</td>
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<tr>
<td>Visual hallucinations and transient obscuration with or without migraine (14,15)</td>
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<th>Brainstem lesions</th>
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<tr>
<td>Unilateral internuclear ophthalmoplegia (16)</td>
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<tr>
<td>Bilateral internuclear ophthalmoplegia (17)</td>
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<tr>
<td>Isolated sixth nerve palsy (18)</td>
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<td>Isolated third nerve palsy (present case)</td>
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In systemic lupus erythematosus, the pathogenesis of CNS manifestations has been similarly felt to be due to vaso-occlusive phenomenon in small vessels. As opposed to the characteristic inflammatory cell infiltration of blood vessel walls and fibrinoid necrosis, pathologic studies of patients with CNS lupus infrequently show these features. More typically, a bland vasculopathy with degenerative and proliferative changes in small vessels, similar to those seen in hypertensive encephalopathy, would be present (5, 22).

Since vasculitic lesions are conspicuously absent, alternative explanations for vaso-occlusive phenomenon have been examined. Recent investigations have suggested that even in the absence of local immune complex deposition, profound complement activation can result in a release of chemotactic factors (C3a and C5a) resulting in the aggregation and activation of platelets and neutrophils, with subsequent release of toxic oxygen species and proteolytic enzymes, causing endothelial injury and vascular obstruction (23).

Alternatively, thrombotic and/or embolic events related to the presence of anti-phospholipid antibodies (lupus anticoagulant, anti-cardiolipin) have been postulated (24). Other less likely causes of vascular compromise might include embolic phenomenon related to the presence of verrucous (Libman-Sachs) endocarditis (25) and the presence of thrombotic thrombocytopenic purpura, which has been documented in a number of patients with lupus (26).

This patient’s serologic abnormalities and subsequent course satisfies ARA criteria for the diagnosis of systemic lupus erythematosus (27). However, her initial presentation was most uncharacteristic of patients with CNS involvement. Although neuropsychiatric manifestations may occur before or after the diagnosis of lupus is made, in only ~5% of patients are they the sole presenting features of the disease (28). In the series of Feinglass (3), among 33 patients with neuropsychiatric manifestations preceding or occurring in the first year subsequent to the diagnosis of lupus, 32 had associated clinical symptoms or findings more suggestive of lupus. Furthermore, among those patients with cranial nerve findings, 88% had other acute neurologic features (3). The patient described here reported no other manifestations of lupus until 1 year after her initial presentation.

The use of corticosteroids in this patient was predicated on not only the ocular palsy, but the serologic and CSF abnormalities suggesting more generalized lupus activity and possibly diffuse cerebral dysfunction. The patient’s rapid improvement and benign course may indicate responsiveness to corticosteroid therapy. Since vasculopathic palsy often resolves spontaneously in 4–12 weeks without treatment, we cannot be certain if this may have occurred, similar to the patient reported by Sedwick and Burde (18).

Although some series have shown no alteration in morbidity (3), neuropsychiatric manifestations of systemic lupus erythematosus are generally regarded as a poor prognostic indicator, with cranial neuropathy having a particularly low 5-year survival rate (4). However, when cranial neuropathy presents in isolation, unassociated with signs of generalized cerebral dysfunction and without evidence of significant visceral involvement, the clinical course may be surprisingly benign. In 3 years of continued care, our patient has shown only minor extraneurologic manifestations of lupus and continues to thrive with only symptomatic therapy.

REFERENCES


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