Bilateral Ocular Paralysis

Analysis of 31 Inpatients

James R. Keane, MD

To my knowledge, no general study of complete ophthalmoplegia is available. This study was performed to determine the seats and causes of bilateral ocular paralysis. The personal records of 13,440 neurology and neurosurgery inpatients were reviewed. Eighteen (58%) of 31 patients had Fisher syndrome (13 cases) or Guillain-Barré syndrome (5 cases). Four cases resulted from midbrain infarction, 3 from myasthenia, and 1 each from pituitary apoplexy, skull base metastasis, botulism, mucormycosis, phenytoin toxicity, and trauma. Many conditions produce complete ophthalmoplegia on rare occasions, but Fisher syndrome, which paralyzes the eyes in nearly one third of cases, was by far the commonest cause.

Arch Neurol. 2007;64:178-180

In 1888, W. R. Gowers wrote

Paralysis of all the muscles of both eyes, internal and external, while theoretically conceivable from disease at the neighborhood of the orbital fissure and optic foramen on each side...is practically only met with in cases of nuclear disease. Whether acute multiple neuritis ever involves the ocular nerves we do not know; the possibility that such peripheral neuritis may simulate central disease must be borne in mind.1

Complete bilateral ocular paralysis is a rare condition, usually reported as single cases. As no general study is available to my knowledge, I reviewed my experience to determine the causes and locations of conditions immobilizing both eyes.

RESULTS

Complete ophthalmoplegia occurred in 31 patients (0.2% of my patients). Their ages ranged from 3 to 73 years, with a mean age of 49 years; 22 (71%) were men. The pupils were fixed in 16 cases (<H110225mmin13 cases), partially involved in 8, and spared in 7. Two patients with Fisher syndrome developed oval, reactive pupils. Ptosis was complete in 25 cases, partial in 5, and absent in 1.

Cranial nerve involvement, aside from the ocular motor nerves, occurred in 17 patients and included optic neuropathy in 4 cases bilaterally and 2 unilaterally; unilateral 5th-nerve impairment in 1 case; and bilateral involvement of the 7th nerves in 9 cases, the 10th nerves in 4 cases, the 11th nerves in 3 cases, and the 12th nerves in 2 cases.

Fisher syndrome (13 cases) and Guillain-Barré syndrome (5 cases) were the leading causes of ophthalmoplegia, together composing 18 (58%) of 31 cases. (Ocular paralysis occurred in 31% of my
cases with Fisher syndrome and 3% of those with Guillain-Barré syndrome (Table 1). Midbrain-thalamic infarcts were responsible for 4 cases (3 from atherosclerosis and 1 with cryptococcal meningitis associated with dermatomyositis), 3 cases had myasthenia, and there was 1 case each with orbitosinus mucormycosis, foodborne botulism, pituitary apoplexy, renal carcinoma metastasizing to the skull base (clivus-cavernous sinuses and posterior orbits), acute phenytoin toxicity, and automobile trauma with fractures through the cavernous sinuses and orbits.

Sites of involvement included polyneuropathy in 18 cases, the brainstem in 5, the neuromuscular junction in 4, cavernous sinuses and posterior orbits in 3, and the cavernous sinuses in 1 (Table 2).

### Table 1. Etiology of Complete Bilateral Ophthalmoplegia

<table>
<thead>
<tr>
<th>Cause</th>
<th>Patients, No. (%) (n = 31)</th>
<th>Pupils, No.</th>
<th>Patients With Ptosis, No.</th>
<th>File Patients, No.*</th>
<th>File Patients With Ophthalmoplegia, %†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T (n = 17)</td>
<td>P (n = 6)</td>
<td>N (n = 8)</td>
<td>T (n = 25)</td>
<td>P (n = 4)</td>
</tr>
<tr>
<td>Fisher syndrome</td>
<td>13 (42)</td>
<td>5</td>
<td>6</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Guillain–Barré syndrome</td>
<td>5 (16)</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Midbrain infarction</td>
<td>4 (13)</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Myasthenia</td>
<td>3 (10)</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Pituitary apoplexy</td>
<td>1 (3)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Metastasis</td>
<td>1 (3)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mucormycosis</td>
<td>1 (3)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Botulism</td>
<td>1 (3)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Phenytoin toxicity</td>
<td>1 (3)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Trauma</td>
<td>1 (3)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviations: N, normal pupils or eyelids; P, partial involvement of pupils or eyelids; T, fixed pupils or complete ptosis.

*Total number of patients in my files with each diagnosis.
†Percentage of all of the patients in my files with complete ophthalmoplegia.

### Table 2. Location of Lesions Causing Complete Ophthalmoplegia

<table>
<thead>
<tr>
<th>Location</th>
<th>Cases, No. (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerves, nonlocalized</td>
<td>18</td>
</tr>
<tr>
<td>Brainstem</td>
<td>5</td>
</tr>
<tr>
<td>Neuromuscular junctions</td>
<td>4</td>
</tr>
<tr>
<td>Cavernous sinuses and orbits</td>
<td>4</td>
</tr>
</tbody>
</table>

POLYNEUROPATHY

The high proportion of patients with Fisher and Guillain-Barré syndromes in this series reflects the fact that nearly one third of patients with Fisher syndrome develop complete ophthalmoplegia3 (Table 1). Indeed, Fisher syndrome is one of the few conditions—along with neurotoxic snake4 and tick5 bites—that commonly produce complete ocular paralysis. Cephalic tetanus6 is an occasional cause of bilateral ocular paralysis, but diabetic cranial neuropathy, one of the commonest causes of diplopia and an occasional cause of cranial polyneuropathy,7 very rarely causes complete bilateral ophthalmoplegia.8

MUSCLE AND NEUROMUSCULAR JUNCTION

Impairment of neuromuscular transmission would seem to be a parsimonious route to ophthalmoplegia, but only 1% of my patients with myasthenia and 6% of those with botulism (Table 1) had complete ocular paralysis. Neurotoxins are more effective at blocking the neuromuscular junctions of eye muscles, acting presynaptically in tick bite paralysis5 and through presynaptic or postsynaptic effects in snake envenomation.4

Thyroid eye disease, among the commonest causes of diplopia in eye clinics, rarely produces sufficient tethering and weakness of the extraocular muscles to eliminate all eye movements. In contrast, amyloidosis is an uncommon condition that paralyses the eyes out of proportion to its rarity.9 Many cases of congenital ocular fibrosis and congenital myopathic ophthalmoplegia exhibit minimal or absent eye movement whereas progressive external ophthalmoplegia exhibits slowly progressive ocular limitation that occasionally becomes complete.

CAVERNOUS SINUS AND ORBITS

A 1964 review10 of skull base lesions found 14 cases of complete bilateral ophthalmoplegia caused by tumors and 5 cases with vascular causes. Tumors included 5 originating in the pituitary or hypophysis, 3 metastases (lung, breast, and ovarian primary tumors), 2 sinus malignancies, 2 of indeterminate nature, 1 lymphoma, and 1 nasopharyngeal malignancy. Vascular causes consisted of 2 cases of carotid-cavernous fistulae, 1 case with combined effects of fistula and repair, 1 supraclinoid carotid aneurysm crossing the midline (with incomplete paralysis), and 1 case of paired cavernous carotid aneurysms.10

More recent reports include malignancies involving the cavernous sinuses (lymphoma,11,12 pituitary carcinoma,13 sphenoid sinus adenocarcinoma,14 and metastases...
from prostate carcinoma\textsuperscript{15} and mesenteric liposarcoma\textsuperscript{16}, skull base (parathyroid metastasis\textsuperscript{17}), and meninges (lymphoma\textsuperscript{18}). Exceptionally, benign involvement of the skull base with fibrous dysplasia can result in ocular paralysis.\textsuperscript{19}

Vascular causes include carotid-cavernous fistulae\textsuperscript{20} and bilateral orbital infarction associated with antiphospholipid antibody syndrome.\textsuperscript{21} Meningitis is a surprisingly rare cause of complete bilateral ophthalmoplegia,\textsuperscript{22} as is bacterial cavernous sinus thrombophlebitis,\textsuperscript{23} but sino-orbital-cavernous fungal diseases (mucormycosis,\textsuperscript{24,25} or less commonly, aspergillosis\textsuperscript{26} or actinomycosis\textsuperscript{27}) disproportionately paralyze the eyes through infarction and inflammation.

**BRAINSTEM**

Coma often obscures ophthalmoplegia in central lesions of the midbrain, but rarely, strokes,\textsuperscript{28,29} abscess,\textsuperscript{30} viral encephalitis,\textsuperscript{31,33} and paraneoplastic encephalitis\textsuperscript{34-36} paralyze both eyes. Occasionally, progressive supranuclear palsy, Whipple disease, and even multiple sclerosis render the eyes immobile, largely through supranuclear mechanisms. Wernicke disease produced complete ophthalmoplegia in 3\% of cases in a large series,\textsuperscript{37} and experimental Wernicke disease typically progresses to complete ophthalmoplegia.\textsuperscript{38} The rare ophthalmoplegic brainstem toxicity of drugs (especially phenytoin and carbamazepine) frequently produces caloric-fast, reversible ocular paralyses.\textsuperscript{39} Frequently, ophthalmoplegia in a diabetic patient with a sensory-motor distal polyneuropathy.

Accepted for Publication: January 13, 2006.

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**Financial Disclosure:** None reported.

**REFERENCES**