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.

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.

METHODS

From personal records of 13,440 inpatients who were personally examined in the wards of the Los Angeles County/University of Southern California Medical Center during a 34-year period, I selected those without perceptible movement in either eye. Comatose patients were excluded. Seven of the patients have been described previously.2 Photographs available for review included 21 slides, 4 video segments, 1 movie clip, and 1 fundus photograph. Diagnoses were established by history, physical examination, and contemporary laboratory and radiological tests. Guillain-Barré syndrome was distinguished from Fisher syndrome by the presence of definite limb weakness. Clinical and radiographic findings provided localization.

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 (≈1/3 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

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cases with Fisher syndrome and 3% of those with Guillain-
Barre´ syndrome [Table 1]. Midbrain-thalamic in-
farcts were responsible for 4 cases (3 from atherosclero-
sis 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 metastasa-
sing to the skull base (clivus-cavernous sinuses and pos-
terior 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).

## COMMENT

### POLYNEUROPATHY

The high proportion of patients with Fisher and Guillain-
Barre´ syndromes in this series reflects the fact that nearly
one third of patients with Fisher syndrome develop com-
plete ophthalmoplegia3 (Table 1). Indeed, Fisher syn-
drome is one of the few conditions—along with neuro-
toxic snake4 and tick5 bites—that commonly produce
complete ocular paralysis. Cephalic tetanus6 is an occa-
sional cause of bilateral ocular paralysis, but diabetic cra-
nial neuropathy, one of the commonest causes of diplo-
pia 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. Neu-
rotoxins are more effective at blocking the neuromus-
cular junctions of eye muscles, acting presynaptically in
tick bite paralysis5 and through presynaptic or postsyn-
aptic effects in snake envenomation.4

Thyroid eye disease, among the commonest causes of diplopia in eye clinics, rarely produces sufficient tether-
ing and weakness of the extraocular muscles to eliminate
all eye movements. In contrast, amyloidosis is an uncom-
mon condition that paralyzes 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 oph-
thalmoplegia exhibits slowly progressive ocular limita-
tion that occasionally becomes complete.

### CAVERNOUS SINUS AND ORBITS

A 1964 review10 of skull base lesions found 14 cases of com-
plete bilateral ocular paralysis 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 in-
determinate 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 carcino-
ma,13 sphenoid sinus adenocarcinoma,14 and metastases
from prostate carcinoma,\textsuperscript{15} mesenteric liposarcoma,\textsuperscript{16} skull base (parathyroid metastasis),\textsuperscript{17} and meningitis (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 fistula\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{30,31} viral encephalitis,\textsuperscript{32,33} 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 paralysis.\textsuperscript{39} As is bacterial cavernous sinus thrombophlebitis,\textsuperscript{23} from prostate carcinoma,\textsuperscript{15} and mesenteric liposarcoma,\textsuperscript{16} skull base (parathyroid metastasis),\textsuperscript{17} and meningitis (lymphoma).\textsuperscript{18} Exceptionally, benign involvement of the skull base with fibrous dysplasia can result in ocular paralysis.\textsuperscript{19}

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**REFERENCES**