nctions between cortex, limbic system, hypothalamus and brain stem, as experimental stimulation of such structures demonstrates.

Autonomic symptoms are more frequently reported in temporal lobe epilepsy, but this may only be because consciousness is generally preserved. In common with other types of seizure, bradyarrhythmias are less prevalent than tachyarrhythmias. Simultaneous EEG and ECG monitoring of the present patient's attacks did not prove possible, but was achieved in two of the three previously reported instances of sinoatrial arrest during temporal lobe seizures. In these, asystole occurred shortly after seizure onset and lasted for 8 to 10 seconds prior to the development of a generalised convulsion. The earliest reported patient also showed abrupt asystole, lasting for up to 8 seconds, following an epigastric aura or angor ani. In the present case, termination of the astyolic episodes by atropine confirms that they were neurally mediated.

There was no past history of simple syncope, and the onset of bradycardia was always preceded by dèja vu. He had had other dèja vu attacks without cardiac sequelae, and was found to have temporal lobe EEG abnormalities and a tumour presumed responsible for these. We therefore feel confident that temporal lobe epilepsy was the primary cause of his astyolic episodes, and that only the subsequent loss of consciousness and jerking could have been attributable to cardiac-induced cerebral ischaemia. Whether or not the hypothalamic distortion produced by the tumour predisposed to autonomic dysfunction is not clear.

The importance of detecting primary cardiac arrhythmia in cases of both non-epileptiform and epileptiform attacks is well established. The reverse situation, that of significant cardiac arrhythmia caused by primary epileptic disturbance, may be more common than generally supposed. Awareness of this possibility, supported where needed by combined ECG and EEG monitoring, will help avoid one of the potentially fatal consequences of an otherwise relatively benign condition. Moreover where, as in this case, a structural lesion is responsible, it can be removed.

References


Mental status changes induced by eye drops in dementia of the Alzheimer type

SIR: Topical administration of eye drops can produce serious systemic complications in the pulmonary, cardiovascular, musculoskeletal and central nervous system. Dementia of the Alzheimer type patients are particularly vulnerable to these side effects because of the known neurochemical abnormalities that occur in this disorder. Recent work has demonstrated reduced activity of choline acetyltransferase and acetylcholinesterase in biopsy and post-mortem brain tissues of affected patients. Other neuropeptides and neurotransmitters may also be significantly altered in dementia of the Alzheimer type. Toxic reactions from ophthalmic agents may unmask or increase the cognitive deficits, behavioural and personality changes which clinically characterise dementia of the Alzheimer type.

Clinical reports have documented central nervous system (CNS) reactions such as confusion, hallucinations, ataxia, agitation, dystarthis and psychosis after the use of anticholinergic eye drops. Cholinomimetic agents such as pilocarpine and aceclidine are generally administered to reduce intraocular pressure in patients with certain types of glaucoma. Their clinical use has not been associated with mental changes although pilocarpine has been shown to produce complex behavioural and electrophysiological alterations in experimental animals. We report three patients who developed CNS manifestations following pilocarpine administration and were subsequently found to have dementia of the Alzheimer type.

Three elderly patients were referred to the Dementia Clinic of Thomas Jefferson University Hospital for progressive cognitive dysfunction following administration of ophthalmic drops. They had a normal medical evaluation, which included: complete blood count, sedimentation rate, thyroid, renal and liver function tests, serum Vitamin B12 and folate levels, electrolytes, urinalysis, electrocardiogram and chest radiograph. Neurological studies consisted of computed tomography (CT) of the brain, electroencephalogram (EEG) and cerebrospinal fluid (CSF) studies in all patients. Cerebral digital subtraction angiography and neuro psychological testing were done in cases 2 and 3 and magnetic resonance imaging (MRI) in case 1. All patients underwent several complete neurological examinations.

Case 1 was a 72-year-old, right-handed, white male, who presented with a 5 year history of progressive decline in short term memory and episodes of confusion and irritability, especially at night. His symptoms started after he was treated with 4% pilocarpine and 2% epinephrine eye drops for glaucoma. At that time, he also had visual hallucinations and lability of affect. He was treated with haloperidol, but this was discontinued because of tremors. His wife and daughter reported intermittent visual hallucinations and mood swings within an hour after each application of the ophthalmic medications. Neurological examination revealed an alert, elderly man, who was oriented only to person. He had no insight into his medical illness and his recent and remote memory were markedly impaired. The patient was unable to do serial 7s, name fingers, draw objects and follow a four-part command. He had a labile affect and right-
left confusion. He could write his name and read. His pupils were constricted and the
fundus could not be visualised. His hearing,
speech and swallowing were normal. His
face was symmetrical and sensation on both
sides of the face was intact. He walked with
short steps and a slightly broad-based gait.
He could not do tandem walk. Cog-wheel
rigidity, bradykinesia and tremors were
absent. He had normal muscle strength and
sensation. He had mild diminution of
vibration sensibility in both feet. His deep
tendon reflexes were 2+ bilaterally and his
plantar responses were flexor. Snout, pal-
momentar and glabellar reflexes were posi-
tive. He had no difficulty with bowel or blad-
der control and there was no family history
of dementia.

Case 2 was a 76-year-old, right-handed,
white female, who was brought by her fam-
ily for “decreasing memory”. Her family
 traced the onset of her symptoms to cataract
surgery performed 4 years prior to consul-
tation. During that hospitalisation, she
became confused and agitated following
administration of 2% pilocarpine and
isoptic eye drops. Her family claimed that
after discharge, she developed progressive
memory loss and irritability. On neuro-
ological examination, the patient was
markedly demented and disoriented to per-
sion, place and time. She did not remember
her age, address, or the names of her chil-
dren. She was not aware of any medical
problem. She had severe recent and remote
memory impairment. She was unable to do
simple calculations, write her name, name
common objects and body parts, copy sim-
ple figures and distinguish left and right
body parts. She demonstrated mood swings
during her examination. The pupils were
2mm and equally reactive to light and to
accommodation. Horizontal and vertical
eye movements were full. Fundi were
benign. She did not have dysarthria, dys-
phagia or hearing loss. Her face was sym-
metrical and she felt pin prick on both sides
of the face. Her tongue was in the midline.
She had moderately increased muscle tone
in all extremities, more pronounced on the
right. She had no weakness of any muscle
group. Cog wheel rigidity and tremors were
not appreciated. Cerebellar examination
demonstrated bilateral impairment of finger
to nose movements, rapid alternating move-
ments, fine finger movement and heel to shin
coordination. Deep tendon reflexes were
symmetrical and her plantar responses were
flexor. She had snout, glabellar and grasp
reflexes. She denied any urinary or bowel
incontinence. There was no family history of
dementia.

Case 3 was a 77-year-old, right-handed,
retired male physician, who referred himself
for intermittent “disorientation, short term
memory loss, apprehension and inability to
keep still.” According to his wife, his symp-
toms began 3 months earlier following tra-
beculectomy for primary open angle glau-
coma. At that time, he was given
isoptocarpine 2%, epirin 2% and maxitrol
suspension. He continued to take the first
two medications until the neurological eva-
ulation. Neurological examination revealed
an agitated, but well oriented male with
marked recent memory loss. His remote
memory was intact. He had difficulty with
serial 7s and he followed four-part com-
mands with hesitancy. His problem inter-
pretation was concrete. He could read,
write, name objects, body parts and colours.
His speech was normal. He had difficulty
copying simple figures. The pupils were
2.5mm in diameter, equal and reactive to
light and accommodation. The extracoloar
movements were full. He had normal visual
fields by confrontation and fundi. Speech,
swallowing, hearing and gag reflexes were
unremarkable. His face was symmetrical
with intact sensation to pin prick, light
touch and temperature. Gait, muscle tone
and strength were normal. He had no cog
wheel rigidity, bradykinesia or tremor. Sen-
sory examination to pin prick, light touch,
vibration and position were intact. Deep
tendon reflexes were normoactive and the
plantar responses were flexor. Snout, gla-
bellar and grasp reflexes were negative. He
had mild bilateral dysmetria on finger to
nose testing. He had slight difficulty with
tandem walking. Romberg's test was nega-
tive. He had no bowel or urinary inconti-
ence. There was no family history of
dementia.

The presenting manifestations of our
cases included memory loss, hallucinations,
lability of affect, confusion and agitation.
These symptoms were initially observed by
relatives and attending ophthalmologists
within hours after the patient received eye
drops for primary open angle glaucoma. No
pulmonary and cardiovascular complaints
were reported. Pilocarpine eye drops were
given to every patient and epinephrine to
case 1 and 3. Maxitrol, an antibiotic sus-
pension was also prescribed to case 3.
Pilocarpine was discontinued in all patients
after neurological evaluation.

The neurological diagnosis in all cases
was dementia of the Alzheimer type. Visual
hallucinations and lability of affect disap-
ppeared in case 1 and agitation was markedly
diminished in case 3 after pilocarpine was
withdrawn. Case 3 did not show any change
in clinical status. Except for a slight increase
of right sided muscle tone and dysmetria in
carinac action, is a commonly prescribed eyedrop for middle aged and elderly patients.

In dementia of the Alzheimer type, deterioration of intellectual function and behavioural changes have been linked to the neurochemical deficiency and morphological lesions involving the cholinergic system. Diminished activity of choline acetyltransferase is believed to result in acetylcholine deficiency while the loss of cholinergic neurons in the nucleus basalis of Meynert is thought to decrease cholinergic input into different cortical and subcortical regions.21 If we relate these hypotheses to our cases, we can speculate that a chronic low level of muscarinic receptor stimulation occurs in dementia of the Alzheimer type. In such a situation, pilocarpine could induce muscarinic receptor hyperactivity or supersensitivity in some patients with dementia of the Alzheimer type and give rise to mental status changes. This proposed mechanism will have to be verified by future appropriately designed clinical and animal studies.

PATRICIO F REYES* BOYD A DWYER ROBERT J SCHWARTZMAN† THOMAS SACCHETTI‡
*Department of Neurology and Pathology, Jefferson Medical College, and VA Medical Center, Coatesville PA
†Department of Neurology, Jefferson Medical College, Philadelphia PA
‡Department of Psychiatry and Human Behavior, Jefferson Medical College, Philadelphia, USA

Address for correspondence: Patricio F Reyes, M.D., Assistant Professor of Neurology & Pathology, Jefferson Medical College, 1020 Locust Street, #278 Philadelphia, Pennsylvania 19107, USA.

References


11 Carpenter WT. Precipitous mental deterioration following cycloplegia with 0.2% cyclopleptolate HCl. Arch Ophthalmal 1967;78:445-7.

Accepted 26 March 1986

Matters arising

Age-specific incidence rates for motor neuron disease

Sir: The recent paper by Li, Swash and Alberman1 states that they are not aware of previous estimates of age-specific rates in motor neuron disease. We originally reported in 19802 that age-specific incidence rates for motor neuron disease rise with increasing age. We presently have a paper in press which updates our previous study and confirms this finding.3 Although the authors report theirs is the first age-specific incidence figure in motor neuron disease, they have been reported prior to our 1980 paper.4

The use of hospital admissions as the source of cases implies that the diagnosis of motor neuron disease will always be made and recorded. This may be true for younger patients; however, elderly patients, particularly those in nursing homes, are less likely to be hospitalised and are more likely to have multiple disease involvements, such as cardiovascular, and pulmonary, which may obscure the diagnosis of motor neuron disease. A greater proportion of overlooked diagnoses of motor neuron disease is likely among elderly patients.

In our experience as well as that of Li et al, the rise in incidence was not apparent in women aged over 80 years. The numbers are small and the possibility exists that motor neuron disease is more commonly overlooked in elderly women. Thus, the significance of this finding is not now obvious and deserves further study.

We agree that the findings of Li et al are important and support our observation that the age-specific incidence rates of motor neuron disease increase with advancing age.

LEONARD T KURLAND, M.D. DR.P.H
DONALD W MULDER, M.D
Mayo Clinic and Mayo Foundation,
200 SW First Street,
Rochester, MN, 55905 USA

References

3 Jurgens SM, Kurland LT, Okazaki H, Mulder