Reversible downbeat nystagmus and ataxia in felbamate intoxication

Ty-Long Huang, MD; Charles N. Still, MD; and J. Eric Jones, MD

Felbamate is a newly available antiepileptic agent useful as monotherapy and adjunctive therapy in adults with partial seizures and in children with Lennox-Gastaut syndrome. Although dose-dependent cerebellar dysfunction is common with other anticonvulsants, this has occurred with felbamate only in add-on trials in which the dysfunction was plausibly linked to increases in the level of the primary anticonvulsant. We report a case of felbamate intoxication associated with ataxia, downbeat nystagmus, and behavioral changes.

Case report. A 44-year-old man was admitted to the hospital on May 11, 1994, because of unsteady gait and falling. He had a history of left frontotemporal contusion in July 1993, with subsequent development of complex partial seizures. Phenytoin was prescribed for his seizure disorder; he was subsequently admitted twice for episodes of phenytoin toxicity with ataxia and agitation. The psychiatric consultant felt that these were part of a pattern of behavior consistent with a diagnosis of factitious disorder. Four weeks prior to admission, the patient’s medication was switched from phenytoin to felbamate to prevent future episodes of self-induced toxicity. The dosage of felbamate was finally increased to 1,200 mg tid. Several days before admission, he surreptitiously obtained a 10-day “emergency” supply of 60 600-mg felbamate tablets. The staff of the residential home where he resided observed that he was “popping” felbamate. His other medications included haloperidol 1 mg tid and benztrapine 1 mg bid. The admission examination showed that the patient was oriented to person, time, and place. He was agitated and belligerent, accusing the physician of improperly prescribing his antiepileptic drugs. The pupils were of equal size and normally reactive to light. There was a constant downbeat nystagmus in primary position and in downward gaze. His eyes did not follow the examiner’s finger in any direction, except slightly in the downward direction. Spontaneous horizontal saccades to either side were present. No downbeat nystagmus was observed in upward or lateral gaze. There was no evidence of extracocular disease. He had generalized mild motor weakness, and rapid alternating movements of the hands and feet were slowed. The heel-shin test showed slight dysmetria. His gait was ataxic with a wide base, and he required assistance in walking. The remainder of the examination was unremarkable.

Admission laboratory studies that were normal included complete blood count, electrolytes, renal and liver functions, calcium, magnesium, and Westergren erythrocyte sedimentation rate. Rapid plasma reagin was nonreactive. Ethanol serum level was zero and phenytoin serum level was <0.5 mg/l. On the day after admission, 21 hours after felbamate was withheld, the patient’s felbamate plasma level was 110 mg/l. Downbeat nystagmus disappeared 1 day later. Agitation, belligerence, and ataxia resolved over the next 5 days. Because of the patient’s severe behavioral disturbance, haloperidol was increased and sertraline was added on the second hospital day. Felbamate was resumed at a lower dose of 2,400 mg/d on the third hospital day. Four days after admission, the patient was able to walk well, and he appeared calmer and less belligerent.

MRI of the brain showed an old right temporal encephalomalacia, a lacunar infarct in the right basal ganglia, and small high signal intensity lesions in the right centrum semiovale. There was no lesion in the cervical-medullary junction, brainstem, or cerebellum.

Discussion. This patient presented with agitation, ataxia, and downbeat nystagmus after he was observed taking an overdose of felbamate tablets. Agitated behavior had also occurred with previous episodes of phenytoin toxicity, and may reflect his concurrent psychiatric illness. The felbamate plasma level was high (110 mg/l) 21 hours after felbamate was withheld. As previously reported for patients taking 3,600 mg/d of felbamate as monotherapy, the mean (±SD) plasma concentrations of felbamate were 63 ± 18 mg/l. Since the half-life of felbamate as monotherapy is 19 to 20 hours, our patient’s blood level of felbamate probably was much higher than 110 mg/l at the time of admission.

Downbeat nystagmus suggests dysfunction of the caudal medulla and archicerebellum. The most common causes are Arnold-Chiari malformation and cerebellar degeneration. Other causes include infarction of brainstem or cerebellum, head trauma, multiple sclerosis, encephalitis, syringobulbia, toxic substances (lithium intoxication, alcohol and toluene abuse), metabolic causes (magnesium depletion, Wernicke’s encephalopathy, vitamin B12 deficiency), or a transient finding in normal infant. Other anticonvulsants such as phenytoin and carbamazepine also cause downbeat nystagmus. Since none of these disorders or medications was present in our patient, we believe that his downbeat nystagmus was a manifestation of felbamate toxicity.

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References

Acute, painful, pupil-involving third nerve palsy in chronic inflammatory demyelinating polyneuropathy

Jorge G. Arroyo, MD, and Jonathan C. Horton, MD, PhD

There are reports of oculomotor palsies in chronic inflammatory demyelinating polyneuropathy (CIDP)1-4 but none clearly describing a pupil-involving third nerve palsy. We report a young woman with CIDP who developed an acute, painful, pupil-involving third nerve palsy.

Case report. This 31-year-old Japanese-American woman had an 11-year history of CIDP characterized by recurrent episodes of weakness in her extremities, tingling and numbness of the hands and feet, gait unsteadiness, and difficulty swallowing. She met the diagnostic criteria for CIDP, with areflexia, features of demyelination on electrophysiologic testing, and an elevated CSF protein (226 mg/dl).5 No evidence was found for diabetes mellitus or any other systemic disease. A chest x-ray, complete blood count, sedimentation rate, antinuclear antibody test, rheumatoid factor, thyroid function studies,
levels for creatine kinase, B₁₂, folate, phytanic acid, and a serum protein electrophoresis were all normal. Five months earlier an attempt to wean her from prednisone failed because she developed lower-extremity weakness. Since that episode she had been maintained on 15 mg of prednisone every other day without symptoms.

We were asked to examine her on an emergency basis after she developed over a period of 3 days right periorbital pain, diplopia, and drooping of the right eyelid. Her right pupil measured 8 mm and reacted minimally to light. The left pupil was 4 mm and responded briskly to light. There was ptosis and weakness of adduction, intorsion, and supraduction of the right eye. An MR scan and an MR angiogram were normal. Specifically, there were no demyelinating plaques. Subsequently, we obtained a catheter angiogram of the cerebral circulation to exclude the possibility of a small aneurysm that an MR angiogram might have missed. None was found. We increased the patient's dose of prednisone to 40 mg/d. One week later, her symptoms began to improve. After they resolved entirely over the following month we reduced her prednisone dosage to 15 mg every other day.

Discussion. Although ocular motor nerve involvement is frequent in acute inflammatory demyelinating polyneuropathy, it occurs in only 3 to 4% of patients with CIDP. Reports often fail to specify which ocular motor nerve is affected. Paresis of the abducens nerve is most often described. There are only two published cases of possible third nerve palsy. Waddy et al. reported a 27-year-old woman with a history of ptosis and diplopia, but her palsy resolved prior to their examination. Fleet and Valenstein also recorded a history of multiple episodes of diplopia and ptosis in a 19-year-old man, who came to their attention later when he developed other symptoms of CIDP.

An acute, painful, pupil-involving oculomotor nerve palsy in a young person raises the specter of an intracranial aneurysm. The normal MR angiogram we obtained made an aneurysm unlikely. We suspected that the oculomotor nerve palsy in our patient was due to CIDP, but we were unable to find a clear description of such a case in the literature. Without a precedent for oculomotor nerve palsy in CIDP, we felt compelled to obtain a catheter angiogram to exclude an aneurysm. The negative angiogram and the rapid resolution of our patient's symptoms after increasing her steroid dosage support our conclusion that oculomotor nerve palsy can occur as a manifestation of CIDP.

From the Department of Ophthalmology, University of California, San Francisco, CA.

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Address correspondence and reprint requests to Dr. Jonathan C. Horton, Department of Ophthalmology, University of California, San Francisco, 10 Kirkham Street, San Francisco, CA 94143-0730.

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