Opsoclonus Persisting During Sleep in West Nile Encephalitis

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**Background:** Recent outbreaks of West Nile virus infection have alerted the public to disabling paralysis as an outcome. Ocular motor involvement with West Nile virus is rare.

**Objective:** To describe a patient with West Nile virus encephalitis that resulted in opsoclonus-myoclonus syndrome with persistent ocular oscillation on electroencephalography during stage 2 sleep.

**Patient:** A 53-year-old man who presented with viral prodrome followed by intense vertigo and encephalopathy. In addition to multifocal myoclonic jerks in the extremities, his eye movements were disrupted by bursts of high-frequency, conjugate ocular oscillations that occurred in random directions.

**Results:** Electroencephalography showed eye movement artifacts during the awake state and stage 2 sleep. Opsoclonus-myoclonus syndrome remained disabling 3 months after onset but markedly improved 8 months after onset.

**Conclusions:** West Nile virus is another cause of opsoclonus-myoclonus syndrome that can occur in conjunction with encephalitis. The presence of an eye movement artifact on results of electroencephalography during stage 2 sleep should raise suspicion for opsoclonus.

Arch Neurol. 2006;63:1324-1326

Although 80% of West Nile virus (WNV) infections are asymptomatic, infected patients may present with a variety of clinical neurological manifestations. In this report, we describe a serologically confirmed case of WNV encephalitis with opsoclonus-myoclonus syndrome (OMS) in which the patient showed persistent ocular oscillations during stage 2 sleep, remained disabled 3 months after the onset of his illness, and markedly improved 5 months thereafter.

**REPORT OF A CASE**

A 53-year-old man with chronic hypertension, coronary artery disease, and left leg traumatic amputation presented with malaise and irritability of 2 weeks' duration followed by high fever (temperature, 40.5°C), dysuria, and severe frontal and cervical pain. A urinary tract infection was diagnosed and gatifloxacin (Tequin) was administered, but the patient showed no improvement. A few days prior to hospitalization, he developed involuntary eye movements and jerking of the muscles in his upper limbs, along with intense, brief attacks of vertigo. On examination, the patient was an ill-looking, tremulous man with neck stiffness. He was hemodynamically stable and had no rash or lymphadenopathy. He had a fluctuating clouding of consciousness with confusion. There were no signs of meningeal irritation. His language was normal but he exhibited scanning speech. Muscle strength and tendon reflexes were normal and symmetrical, with a flexor right plantar response. There were prominent, involuntary, myoclonic muscle jerks, with intermittent action tremor in the upper extremities. When asked to look at a target, the patient’s visual fixation was disrupted by bursts of high-frequency, conjugate ocular oscillations that had horizontal, vertical, and torsional components, all of which indicated opsoclonus (a video is available online at http://www.archneurol.com). Opsoclonus, but not myoclonus, was present during sleep (see the online video). The rest of the cranial nerve examination results were normal. He was unable to walk. Findings of a computed tomographic scan of the head were normal (a magnetic resonance image could not be obtained because of the patient’s cardiac pacemaker). An analysis of cerebrospinal fluid showed lymphocytic pleocytosis (white blood cell count, 81/µL; 87% lymphocytes, 12% monocytes, and 1% neutrophils), with a total protein level of 0.11 g/dL and a glucose level of 52 mg/dL (3.1 mmol/L). Gram stain and cultures yielded negative results, including stains and

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cultures for fungi and *Toxoplasma gondii*. Polymerase chain reactions did not amplify any of the following viruses: herpes simplex, varicella-zoster, Epstein-Barr, Cytomegalovirus, or *Enterovirus*. Possible cross-react to encephalitis viruses (California, La Crosse, eastern equine, western equine, and St Louis) was eliminated by negative results of viral serology to both IgG and IgM antibodies. The patient had no recent history of travel or prior vaccination to yellow fever or Japanese B encephalitis viruses; thus, no further evaluation of these viruses was sought. Human immunodeficiency serology results were nonreactive. Paraneoplastic autoantibodies (anti-Ri, anti-Hu, anti-Yo, and anti–Ma-2) were undetectable in the serum. Electroencephalography (EEG) while the patients was in the awake state showed a mild slowing of the posterior dominant rhythm, with frequent prolonged runs of eye movements (Figure, B) corresponding to opsoclonus. The eye movements on EEG and the opsoclonus persisted during stage 2 sleep (note the sleep spindles in the Figure, A), although they were less frequent. The patient was initially treated with intravenous ceftriaxone sodium, vancomycin, ampicillin, and acyclovir. The use of these agents was discontinued after the detection of WNV on serologic analysis and after negative polymerase chain reaction results for herpes simplex and varicella-zoster viruses. Enzyme-linked immunosorbet assay results were positive for the presence of IgM antibodies to WNV and negative for the presence of IgG antibodies to WNV in the cerebrospinal fluid (ViroMed Laboratory, Minnetonka, Minn). Titors were not obtained on initial testing. The patient was discharged to a rehabilitation facility.

Three months after disease onset, the patient continued to be debilitated with severe myoclonic jerks and fluctuating alertness due to encephalopathy. Thereafter, he started to improve, and 8 months after disease onset his cognition returned to normal and he was able to walk with the use of a cane. Saccadic intrusions and myoclonic jerks were absent, although mild action tremor was present. Follow-up serology results 8 months after disease onset showed an elevated IgG level of 4.3 (index value, <1.3), elevated IgM level of 1.9 (index value, <0.9), and a markedly elevated WNV neutralizing antibodies level of 1:160 (index value, <1:5) (Focus Diagnostics, Inc, Cypress, Calif).

**COMMENT**

West Nile virus is a single-stranded RNA flavivirus and a member of the Japanese encephalitis virus serocomplex. Rare neuro-ocular invasions cause a variety of ocular syndromes. The ocular findings include multifocal chorioretinitis and optic neuritis. The report of a similar case generating sleep spindles. The published description of 2 patients with spasmodictic atrophy who had slow saccades and abnormal sleep architecture suggested the involvement of neural circuitry in the brainstem. A subsequent study identified a possible switch mechanism, thought to be coordinated by 2 sets of pontine neurons. An alternative hypothesis is that opsoclonus...
The cause of death Thus, there is some doubt as to whether WNV was primarily responsible for the OMS. The second case mimicked the symptoms of our patient (except for the prompt improvement upon hospital discharge) but without a recognized EEG or sleep abnormality.

In summary, we document a case of OMS due to WNV infection in which ocular oscillations persisted during stage 2 sleep. For electroencephalographers, the presence of rapid eye movement artifact during stage 2 sleep should raise the suspicion for opsoconul.

Accepted for Publication: May 1, 2006.

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Author Contributions: Study concept and design: Alshekhlee. Acquisition of data: Alshekhlee, Sultan, and Chandar. Analysis and interpretation of data: Alshekhlee and Chandar. Drafting of the manuscript: Alshekhlee. Critical revision of the manuscript for important intellectual content: Sultan and Chandar. Administrative, technical, and material support: Alshekhlee.

Additional Information: The video is available online at http://www.archneurol.com.

Acknowledgment: We thank John R. Leigh, MD, for his critical review and helpful comments in the preparation of the manuscript.

REFERENCES