NON-CONVULSIVE STATUS EPILEPTICUS IN WEST NILE VIRUS MENINGOENCEPHALITIS: TWO CASES AND REVIEW OF LITERATURE

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ABSTRACT

Background: West Nile Virus (WNV) is an arthropod-borne flavivirus which causes epidemic spread by mosquito bites and its incidence has been ever increasing. Though less than 1% of infections lead to severe neurological involvement, meningoencephalitis is the major cause of morbidity and mortality. There has been little data on the presentation of seizures or non-convulsive status in WNV. We aim to highlight (1) the presentation of nonconvulsive status in WNV infection and (2) value of electroclinical monitoring in its management.

Methods: Literature research was conducted using medline/pubmed for identifying presenting symptoms in WNV encephalitis. Common and uncommon presentations are described. We report two cases of WNV encephalitis with status epilepticus and review electroencephalographic changes and discuss complexities in its management. Pertinent literature on the investigative findings, management and the outcomes is presented.

Results: Electroclinical monitoring revealed patterns consistent with non convulsive status. Antiepileptic medications effectively aborted seizures resulting in clinical improvement. Both patients recovered with minimal neurological impairment and were discharged to rehabilitation facilities.

Conclusions: Neurological complications in the form of seizures due to WNV may be more common than realized. Clinicians should have a high index of clinical suspicion for nonconvulsive status when dealing with WNV infected patients presenting with altered sensorium. Continuous electroencephalographic monitoring is crucial in their management.

Key words: West Nile Virus, meningoencephalitis, seizures, non-convulsive status, EEG monitoring, meningitis, encephalitis

INTRODUCTION

West Nile Virus (WNV) is an arthropod-borne flavivirus in the same taxonomic sub-grouping as Japanese encephalitis virus, St. Louis encephalitis virus, and others [Mackenzie et al, 2004]. Since the first known human case in the West Nile district of Uganda in 1937, WNV has reemerged becoming one of the most widely distributed of all arboviruses. [Smithburn et al, 1940]. The first cases reported in the Western Hemisphere occurred in New York City and surrounding counties in 1999 and included 62 cases of meningoencephalitis and resultant 7 deaths. [Nash et al, 2001]. West Nile virus (an arbo virus) infection has been spreading westward across the continental United States since 1999 (DeSalvo et al, 2004) – Iowa and Nebraska were among the hardest hit states.

While seizures is listed as a neurologic manifestation of WNV neuroinvasive disease in multiple sources, and a known complication of other viral encephalitities, the literature is scant on this issue. In fact, recent electroencephalographic findings in patients with WNV meningoencephalitis indicated a characteristic generalized slowing more prominent in the anterior (frontal and temporal) regions rather than evidence of epileptiform discharges [Gandelman-Marton et al, 2003]. From our study we describe two cases of nonconvulsive status epilepticus associated with WNV meningoencephalitis.

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CASES

Case 1: This is an 81-year-old Caucasian woman was found confused and somnolent in her home on August 23, 2005. She was transported and admitted to her rural area community hospital. The patient was given levofloxacin therapy for a urinary tract infection. Other comorbidities include coronary artery disease with prior stent placement, ischemic cardiomyopathy with prior automatic internal cardioverter-defibrillator placement, hypertension, hyperlipidemia, obstructive sleep apnea, pernicious anemia, diverticulosis, osteoarthritis, and osteoporosis. There was no prior history of seizure activity. While hospitalized, the patient was witnessed to have 30 seconds of generalized tonic-clonic activity. Oral phenytoin was administered without further evidence of clinically apparent seizure activity. She remained confused and drowsy with additional reports of aphasia. On August 31, 2005. She was transferred to the nearest hospital able to provide neurological evaluation including EEG monitoring demonstrating left frontal dominant sharp spike wave discharges. The neurologist began loading intravenous phenytoin therapy. Patient was transferred to a tertiary care hospital for further neurological evaluation and continuous EEG monitoring. Repeated EEG monitoring continued to show rhythmic sharp spike waves located mainly in the left hemisphere, consistent with non-convulsive status epilepticus.

Case 2: This is a 25-year-old Caucasian woman with juvenile rheumatoid arthritis (JRA) was "under the weather" for a week before she developed fever and headache requiring admission to the community hospital. She was diagnosed with meningitis and was treated with antibiotics (TMP-SMZ). Worsening of the mental status over a week of hospitalization and a seizure spell prompted a transfer to our tertiary care medical center. MRI done at that time was normal and CSF showed many WBCs while serology was still pending. On admission the patient was intubated because of the altered sensorium and a repeat spinal tap was done. Patient was started on acyclovir since the CSF picture was indicative of an aseptic etiology. An initial MRI showed non-specific signal changes peripherally in the pulvinar of both thalami seen on the FLAIR images but it was not seen subsequently in the repeat imaging 3 weeks later. The EEG done on admission showed generalised slowing of activity with out any seizure focus. All the medications that the patient was on, including methotrexate was discontinued after Infectious Disease and Rheumatology consults. Palavizuimab had been self discontinued by patient a couple of months earlier and the second CSF serology came back as positive for West Nile virus after a week, while the first sample taken at the community center had come back as negative. Patient was started on dilantin because of a seizure spell at the community center despite that she seized again and this second spell was followed by a non-convulsive status confirmed by continuous EEG monitoring.

Both patients were sedated, intubated, and maintained in burst suppression with intravenous midazolam continuous infusion and dosages of intravenous phenytoin. The emergent EEG monitor showed focal left frontal predominance with generalised siezure discharges. While the Computed Tomography of the head of case-I displayed minimal cortical atrophy in frontal lobes bilaterally, case-II's repeat MRI still remained typical for a herpes encephalitis. Both the scans had no evidence of mass effect, midline shift, hemorrhage or hydrocephalus. Serum as well as cerebral spinal fluid studies were obtained on both patients at admission. CSF analysis indicated lymphocytosis, EBV DNA was negative, Enterovirus RNA was negative, VDRL/CSF also nonreactive. Serum WNV IgM and CSF WNV IgM titers were positive, indicative of acute WNV meningoencephalitis. Both patients were managed effectively with midazolam and dilantin and maintained on burst suppression for two days. Both were slowly weaned off midazolam and ventilator support. The recovery process was slow and painful and both the patients were discharged to a rehabilitation facility on achieving an ambulatory functioning with minimal support.

DISCUSSION

Even though severe neurological involvement remains uncommon (in less than 1% of infections) we had a higher suspicion for WNV meningoencephalitis because Omaha falls in the path of travel of the WNV epidemic and hence asked for the second CSF study. The progression of mental status changes was also an important part of the current medical history. Both of our patients were immunocompromised; case-II was immunosupressed by her rheumatological medication while case-I was probably in immunosenescence due to her advanced age. Literature does mention meningoencephalitis being more common in immunosuppressed patients (Kumar et al, 2004, Weiskittel, 2004). The systematic

process of laboratory evaluations to determine viral activity in an immunosuppressed patient is paramount. All the immunosuppresents that case-II was on for her JRA were stopped and the serology on the second CSF sample came back as positive for the WNV IgM. Various medical illnesses such as malignancies, transplants, diabetes, dialysis, AIDS, and patients on steroid therapies have been reported to have suffered from WNV encephalitis. We add to the list our patient with JRA on immunosuppressant therapy.

In addition, a thorough medical history should always be obtained including possible exposures and recent travel (Weiskittel 2004, Prick et al. 2003).The symptomatology would guide one to the common viruses, but history of mosquito bites was the clue in our cases for testing for an uncommon etiology.

Non-convulsive seizures: Our patients were transferred from a regional health center, because of development of altered sensorium and seizures, to tertiary care centers at the University of Nebraska Medical Center and Creighton University Medical Center in Omaha, Nebraska. The seizures were simple partial, focal motor, becoming generalized, electroencephalogram (EEG) was, therefore, requested, which showed generalized slowing without any epileptogenic focus. However a couple of weeks later the patient developed a similar focal seizures becoming generalized and went on to become status. At this point the EEG showed a left frontal epileptogenic focus. We support the suggestion by DellaBadia et al (2004) that when seizures with atypical EEG patterns present during an acute febrile illness in the warmer months, WN encephalitis should be considered.

Imaging: One of the features in case-II was the initial nonspecific signal changes peripherally in the pulvinar of both thalami seen on the FLAIR images. The patient was given acyclovir. Vidwan et al (2003) had reported a similar finding. Diverse spectrum of CNS imaging findings has been reported in patients with WNV encephalitis (Zak et al, 2005). Kraushaar et al (2005) found hyperintensities in the anterior horn cells of the cervical spinal cord, similar to the poliomyelitis, in their patient with flaccid paralysis of the right upper extremity. Bosanko et al (2003) found two of their patients with striking involvement of the substantia nigra. Hyperintensities in the basal ganglia and thalami was noted by Rosas and Wippold (2003). The need for a West Nile virus MRI registry has already been suggested by Robertson and Sejvar (2003).

CONCLUSIONS AND RECOMMENDATIONS

These cases emphasize the value of total teamwork in the assessment, diagnosis, and treatment of an immunosuppressed patient with a viral syndrome. An important recommendation would be to provide the family members of such patients with educational materials on viral illnesses and meningoencephalitis. Health care professionals should have a high index of suspicion for WNV meningoencephalitis in immunocompromised patients with altered sensorium who develope seizures.

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