West Nile virus encephalitis induced opsoclonus-myoclonus syndrome

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Abstract

West Nile virus (WNV) is an arthropod borne neurotropic single stranded RNA flavivirus with <1% developing presenting with neurological disease. Immunocompromised and elderly patients are more prone to developing WNV meningitis or encephalitis. Definitive diagnosis of WNV meningoencephalitis is a combination of clinical suspicion and cerebrospinal fluid (CSF) serology. Forty-eight-year old Caucasian female presented with a sudden onset of altered mental status after being found unresponsive. She was confused with intermittent bouts of alertness/lethargy and unintelligible responses to questioning. Her medical problems included endometrial cancer that was in remission after undergoing a total abdominal hysterectomy with bilateral salpingectomy and postoperative chemotherapy with paclitaxel and carboplatin. Pertinent physical examination revealed muscle strength that was significantly decreased, nuchal rigidity and +2 pitting edema of both lower extremities. Computed tomography and magnetic resonance imaging of the brain were negative for any intracranial pathology. CSF analysis was consistent with aseptic meningitis with all CSF serology being negative except for positive WNV antibody. A few days after being admitted she developed involuntory random movements of her eyes and generalized jerking movements (myoclonus). This was determined to be opsoclonus myoclonus syndrome (OMS) induced by the WNV meningoencephalitis. She then received five consecutive days of plasmapheresis with a significant improvement in her neurological status. Opsoclonus-myoclonus syndrome (OMS) is a rare neurological disorder associated with chaotic multidirectional eye movements, myoclonus and less frequently cerebellar ataxia. OMS affects as few as 1 in 10,000 people per year. The pathogenesis is not fully understood with the majority of cases of opsoclonus-myoclonus syndrome being idiopathic. According to current medical literature there have only been two previous case reports of opsoclonus myoclonus syndrome associated with WNV encephalitis.

Introduction

West Nile virus (WNV) is an arthropod borne neurotropic single stranded RNA flavivirus. The virus is introduced into the host by the vector (Culex mosquito) during its blood meal. WNV originated in the Middle East and Africa but in recent years has reached the United States. From 1999 to 2011, a total of 31,414 cases of WNV were reported in the United States. The 2012 incidence of WNV neuroinvasive disease was 0.3 per 100,000 in the United States. Approximately 45% of WNV cases were reported in Texas, USA. Seasonal outbreaks occur annually but are often quite focal and unpredictable in size and location. The majority of those infected with WNV are asymptomatic and only 20-30% will present with flu like symptoms. Less than 1% of individuals will eventually develop neurological deficits. Neurological deficits associated with WNV infection can be encephalitis, menigitis or flaccid paralysis. Immunocompromised and elderly patients are more prone to developing WNV meningitis or encephalitis compared to the general population. WNV and other arboviral infections should be considered in the differential diagnosis of aseptic meningitis or encephalitis, especially if the geographical area is prone to WNV infection. The definitive diagnosis of WNV meningoencephalitis is a combination of clinical suspicion and CSF serology. Approximately 50% may have significant postviral morbidity for a year following infection. Management of WNV infection consists of supportive measures. We are presenting a very rare case of a immunocompromised patient that developed opsoclonus myoclonus syndrome following WNV encephalitis.

Case Report

Forty-eight-year old Caucasian female presented with a sudden onset of altered mental status after being found unresponsive. She was confused with intermittent bouts of alertness/lethargy and unintelligible responses to questioning. Her medical problems included endometrial cancer that was treated with a total abdominal hysterectomy with bilateral salpingectomy and postoperative chemotherapy (paclitaxel and carboplatin) and dexamethasone. No history of tobacco, alcohol or illicit drug use.

Initial vital signs on admission included a rectal temperature was 41.1 degrees Celsius, tachycardia (heart rate of 108), stage 1 hypertension (blood pressure of 140/61) and tachypnea (respiratory rate of 34). Pertinent physical examination findings revealed a morbidly obese female that was alert but not oriented to person, place or time and only able to answer yes or no to questioning. Her pupils were 3 mm bilaterally, equal round and reactive to light with intact extraocular movements and no nystagmus noted. All cranial nerves were assessed and normal on examination. No motor or sensory deficits to light, touch, pain, position sense or vibration noted. All reflexes such as biceps, knee tendon and Babinski sign were normal. Muscle strength (3/5 all four extremities) but no tremors, or myoclonus. Nuchal rigidity was observed but Kernig and Brudzinski signs were both negative. She also had bilateral +2 pitting edema of lower extremities. The remainder of organ systems of examination was unremarkable. Initial laboratory work-up (Table 1) was unremarkable except hyponatremia and thrombocytopenia. Brain computed tomography (CT) on admission was negative for any acute pathological abnormalities. CT of the abdomen and pelvis was negative for any acute abdominopelvic pathology. The patient was started on ceftriaxone 2 g IV daily, vancomycin 2 g IV twice daily, and acyclovir 1.5 g IV every 8 hours due to our high suspicion of encephalitis. A lumbar puncture with cerebrospinal fluid (CSF) analysis and CSF serology (Table 2) was consistent with aseptic meningitis. The HIV screening test was negative. Magnetic reso-
The onset of myoclonus may precede the opso-
clonus.

The pathogenesis of opsooclusus is unknown
but, one hypothesis suggests that opsooclusus
is due to damage of the omnipause cells in the
nucleus raphe interpositus of the pons.9 This
prevents unwanted saccades by inhibiting
burst neurons in the paramedian pontine
tectoral formation and rostral interstitial
nucleus of Cajal. However, these omnipause
neurons are spared in paraneoplastic opso-
clusus. Another explanation suggests that
opsooclusus may be generated by disinhibition
of the oculomotor region of the fastigial nucle-
us by a process that interferes with the
inhibitory projections of the Purkinje cells of
the deep cerebellar nuclei to the fastigial
nuclei. The pathogenesis is not fully under-
stood, however, an autoimmune pathophysiol-
ogy has been proposed. Autoimmune dysfunc-
tion of Purkinje cells in the dorsal vermis and
subsequent disinhibition of oculomotor fasti-
gial region seems to be the most probable
mechanism.9 The majority of OMS cases are
idiopathic. However, other common causes of
opsooclusus include paraneoplastic, viral brain-
stem encephalitis and drugs.10,11 The oncone-
ural antibodies associated with OMS are anti-
ri antibodies (gynecologic cancers) and, less
frequently, anti-Hu, anti-Yo, and anti-Ma-2

**Table 2. Cerebrospinal fluid analysis.**

| Appearance                  | Clear and colorless |
|-----------------------------|---------------------|
| White blood cell count      | 67/uL (0-5/uL)      |
| Neutrophils                 | 1%                  |
| Lymphocytes                 | 97%                 |
| Monocytes                   | 2%                  |
| Red blood cell count        | 389/uL (0-5/uL)     |
| Protein                     | 131 mg/dL (15-45 mg/dL) |
| Glucose                     | 38 mg/dL (41-70 mg/dL) |
| Corresponding serum glucose | 68 mg/dL (70-100 mg/dL) |

### Discussion and Conclusions

Opsoclonus-myoclonus syndrome (OMS) is a
rare neurological disorder associated with
chaotic multidirectional eye movements,
myoclonus and less frequently cerebellar atax-
ia. OMS affects as few as 1 in 10,000,000 peo-
ples per year.2 The eye movements are charac-
terized by multidirectional, high amplitude,
arrhythmic and conjugate ocular saccadic
intrusions without intersaccadic latency caus-
ing oscillopsia.4 It should not be confused with
nystagmus which is usually unidirectional and
has a slow component.7 Myoclonus may affect
any part of the body and may be evoked by
action, intention, auditory and visual stimuli.
antibodies. Paraneoplastic diseases associated with OMS include small-cell lung, ovarian and breast cancer. Most infectious disease causes involve the central nervous system or a post infection immune mediated process. The post infectious mechanism has been described as a dysfunction of the cell mediated and humoral immune response. This immune mediated process was postulated because the presence of autoantibodies and the response of OMS to immunosuppressive therapy. These autoantibodies are directed towards certain neural antigens. The specific microorganism is rarely identified however OMS has been reported to occur after infection with enterovirus, Borrelia Burgdorferi, streptococcus, Coxsackie virus, Epstein-Barr virus, mumps or West Nile virus.

Opsoclonus myoclonus syndrome can result in significant long term neurological sequelae if either untreated or undertreated. There is no current established treatment for OMS. Therapy options have been directed towards the suppression of antibody formation and the removal of the autoantibodies. Several therapeutic attempts can be utilized to remove the autoantibodies in patients with OMS, such as IVIG, plasmapheresis, and immunoadsorption. Treatment of the underlying disease process is the mainstay of management for OMS. However there is no available data from clinical trials that suggest a definitive treatment strategy. Because the opsoclonus-myoclonus syndrome is so rare, there are no randomized controlled trials to provide guidelines for either symptomatic or disease modifying treatments. According to current medical literature, only two other case reports have reported opsoclonus myoclonus syndrome induced by West Nile virus encephalitis.

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