West Nile virus encephalitis in a young immunocompetent female in Omaha Nebraska

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1. Introduction

One of the most common cause of arbovirus encephalitis in the United States of America (USA) is West Nile virus (WNV) (1). Its distribution in North America is increasing, gradually spreading throughout the entire continental USA. Ever since the outbreak of WNV in New York in 1999, there have been 46,086 reported cases of WNV including 21,574 of neuroinvasive disease reported through 2016. The total number of deaths reported to the Centers for Disease Control and Prevention (CDC) from 1999 to 2016 are 1,888 (9%) and 129 (1%) due to neuroinvasive and non-neuroinvasive disease respectively (2).

In immunocompetent hosts, 70-80% of infected individuals have subclinical disease. However, in less than 1% of people infected by WNV it can become fulminant neuroinvasive disease associated with neurological morbidity. Herein, we discuss a case of neuroinvasive WNV disease with non-specific symptoms in an immunocompetent young female in Omaha. Our patient survived the acute phase of WNV encephalitis but has extended recovery to daily functioning. We also reviewed literature on WNV cases in immunocompetent individuals and to the best of our knowledge only 3 cases have been reported to date. The difference between reported cases and our case is her younger age, bilateral upper and lower extremity paralysis, 30 day hospitalization with significant morbidity leading to a prolonged stay at rehabilitation facility with residual cognitive and gross motor impairment. Usually WNV is not considered a differential in immunocompetent individuals which leads to delay in diagnosis, management and therefore increases mortality and morbidity. Therefore purpose of our case report is to raise awareness of atypical presentations of WNV infection in immunocompetent individuals in non-endemic area to emphasize the importance of early diagnosis and management.

Keywords: West Nile virus, encephalitis, neuroinvasive disease, arbovirus

Summary

One of the most common cause of arbovirus encephalitis in the United States of America (USA) is West Nile virus (WNV). In immunocompetent hosts, 70-80% of infected individuals have subclinical disease. However, in less than 1% of people infected by WNV it can become fulminant neuroinvasive disease associated with neurological morbidity. Herein, we discuss a case of neuroinvasive WNV disease with non-specific symptoms in an immunocompetent young female in Omaha. Our patient survived the acute phase of WNV encephalitis but has extended recovery to daily functioning. We also reviewed literature on WNV cases in immunocompetent individuals and to the best of our knowledge only 3 cases have been reported to date. The difference between reported cases and our case is her younger age, bilateral upper and lower extremity paralysis, 30 day hospitalization with significant morbidity leading to a prolonged stay at rehabilitation facility with residual cognitive and gross motor impairment. Usually WNV is not considered a differential in immunocompetent individuals which leads to delay in diagnosis, management and therefore increases mortality and morbidity. Therefore purpose of our case report is to raise awareness of atypical presentations of WNV infection in immunocompetent individuals in non-endemic area to emphasize the importance of early diagnosis and management.

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1. Introduction

One of the most common cause of arbovirus encephalitis in the United States of America (USA) is West Nile virus (WNV) (1). Its distribution in North America is increasing, gradually spreading throughout the entire continental USA. Ever since the outbreak of WNV in New York in 1999, there have been 46,086 reported cases of WNV including 21,574 of neuroinvasive disease reported through 2016. The total number of deaths reported to the Centers for Disease Control and Prevention (CDC) from 1999 to 2016 are 1,888 (9%) and 129 (1%) due to neuroinvasive and non-neuroinvasive disease respectively (2).

In immunocompetent hosts, 70-80% of infected individuals have subclinical disease. However, in less than 1% of people infected by WNV it can become fulminant neuroinvasive disease associated with significant neurological morbidity (3). Neurological manifestations most commonly reported include meningitis, encephalitis and acute flaccid paralysis. Factors contributing to life threatening disease with WNV include: age > 50 years (4), multiple comorbidities (5), pregnancy and transplantation (6). Common systemic presenting symptoms are fever, chills, nausea, vomiting, headache, macular and papular rash. Neurologic manifestations include nuchal rigidity, photophobia, acute focal weakness, altered deep tendon reflex. The initial presentation of severe disease with WNV is indistinguishable from other causes of meningoencephalitis, which may lead to delay in appropriate diagnostic testing as described below in our case. Initial testing for WNV with IgG/IgM with Polymerase chain reaction (PCR) is often negative due to its short viremic phase (6). The mortality associated with WNV neuroinvasive disease is 8% (7). Significant risk factors for death are those described above; older individuals have subclinical disease. However, in less than 1% of people infected by WNV it can become fulminant neuroinvasive disease associated with significant neurological morbidity (3). Neurological manifestations most commonly reported include meningitis, encephalitis and acute flaccid paralysis. Factors contributing to life threatening disease with WNV include: age > 50 years (4), multiple comorbidities (5), pregnancy and transplantation (6). Common systemic presenting symptoms are fever, chills, nausea, vomiting, headache, macular and papular rash. Neurologic manifestations include nuchal rigidity, photophobia, acute focal weakness, altered deep tendon reflex. The initial presentation of severe disease with WNV is indistinguishable from other causes of meningoencephalitis, which may lead to delay in appropriate diagnostic testing as described below in our case. Initial testing for WNV with IgG/IgM with Polymerase chain reaction (PCR) is often negative due to its short viremic phase (6). The mortality associated with WNV neuroinvasive disease is 8% (7). Significant risk factors for death are those described above; older
age, pre-existing comorbidities, and a compromised immune system. During a largest WNV outbreak in USA out of 221 hospitalized patients, 18% of patients who had encephalitis died, 46% were discharged to acute rehabilitation, 15% were discharged home with assistance, and only 20% successfully return home without assistance (8). Unlike the majority of individuals with WNV infection who are either asymptomatic or develop a self-limited flu-like illness, herein we describe a patient who developed the most severe form of symptomatic illness.

2. Case Report

Our patient is a 35-year-old immunocompetent African American female with a history of alcohol abuse disorder who presented to emergency department with 4 days of fever, nausea and abdominal pain. She received intravenous fluids and was discharged. Subsequently she began to experience headache, fevers, and diplopia 2-3 days later. She was hemodynamically stable with an unremarkable mental status exam. Physical examination was benign, with no nuchal rigidity or focal neurological deficits. Initial laboratory evaluation demonstrated a white blood cell count (WBC) of $4.6 \times 10^3$ cells/µL, lactic acid level of 4.5 mmol/L, aspartate aminotransferase 516 u/L, alanine aminotransferase 229 u/L, phosphorus 2.0 mg/dL, magnesium 1.0 mg/dL. Noncontrast head computed tomography (CT) head was unremarkable. Magnetic resonance imaging (MRI) of the brain with contrast demonstrated T2 and FLAIR signal hyperintensity in the bilateral caudate nuclei, right/left putamen, deep and subcortical white matter of the bilateral parietal lobes (Figure 1). Cerebrospinal fluid analysis (CSF) yielded 13 red blood cells/µL, 183 WBC/µL with a differential of 64% neutrophils, 35% lymphocytes, and 1% monocytes, glucose 56 mg/dL, and protein 116 mg/dL. CSF culture, viral (Herpes simplex, Human herpes, Human parechovirus, Varicella zoster virus) and fungal (Cryptococcus neoformans/gattii) PCR were negative. She was treated empirically for bacterial meningitis with antimicrobials (Vancomycin + ciprofloxacin) and with acyclovir for herpes encephalitis. On hospitalization day 4, the patient became acutely hypoxic with worsening altered mental status. She was subsequently intubated and transferred to the intensive care unit. A repeat MRI of the brain on day 5 showed no changes from the previous MRI. After excluding other causes of altered mental status (i.e. metabolic encephalitis, fungal, viral, or bacterial meningitis) CSF IgM antibodies for WNV came back positive on day 6. The patient was treated symptomatically with intravenous fluids, respiratory support and prevention of secondary infections throughout the hospital course. She remained unresponsive for 11 days and progressively became more alert over the course of the 2 weeks. On day 18 of hospitalization patient was extubated and was discharged to inpatient acute rehabilitation unit on day 31 with cognitive impairment and residual paraparesis. Follow up with the patient revealed that after several months of physical therapy she is still dependent on walker for activities of daily life.

3. Discussion

WNV accounted for 231 cases as of 21 August 2018, with South Dakota reporting the highest number nationally. The total number of cases reported to the CDC in Nebraska is 14 (2). However, the total number of deaths in Nebraska in 2018 reported to the Nebraska Department of Health and Human Services is 2. Interestingly, 36% of seropositive individuals in Nebraska are aged 26-50 and 69% are of male gender (9). Our patient had no history of recent travel and sick contacts.

Despite many published reports of WNV disease in transplant recipients, to the best of our knowledge there has been only three cases reported in < 45-year-old immunocompetent adults without comorbidities. Micatil et al. 2011, reported a case of WNV meningitis in a 39-year-old women in NYC who presented with headache and spluttering. However, she was discharged after 5 days of hospitalization without symptoms (10). Similarly, the 2nd reported case is from Spain, reported by Kaptoul et al. 2007, in a healthy 21-year-old male who presented with fever, headache, nausea and vomiting. This patient was also discharged on day 7 of hospitalization without symptoms (11). The third is a 21-year-old female from Tuscany, Italy, who presented with fever, nausea, vomiting, nuchal...
rigidity and photophobia. Her symptoms improved within 5 days and she was discharged after 10 days of hospitalization without residual symptoms (12). The subject of our current case presented with atypical symptoms which were initially thought to be secondary to alcohol withdrawal and delirium tremens. She remained on CIWA protocol for alcohol withdrawal for the initial 2-3 days. While she was young and had no comorbidities, her history of alcohol abuse with protein calorie malnutrition may have put her at increased risk of neuroinvasive WNV disease. Additionally, the severity and duration of clinical sequelae of WNV meningoencephalitis was prolonged in our patient. She survived the acute phase of WNV encephalitis but has extended recovery to daily functioning when compared to other reported cases to date. Similarities between cases reported earlier and our case include young age, immune competence, and no significant comorbidities. Above described patient were discharged from hospital without cognitive or physical impairment, however our patient even after several months of acute rehabilitation is still walker dependent (Table 1).

Furthermore, clear guidelines for management of life-threatening WNV disease are lacking (13). There have been review articles which tried to summarize some potential treatments (14-16). However, even the Centers for Disease Control’s MNV disease therapeutics revised in February 2018 review has indicated the same. The treatment is mainly supportive. Experimental therapies such as ribavirin, human intravenous immunoglobulin and interferon-alpha have been described in the literature. However, the data supporting their use is limited, which poses a dilemma for physicians who are treating patients with neuroinvasive WNV disease. The purpose of this case report is to raise awareness of atypical presentations of WNV infection in immunocompetent individuals in non-endemic area which leads to delay in diagnosis and management.

4. Conclusion

Given the increasing prevalence of WNV disease in the USA, testing patients' CSF for additional studies include WNV infections in febrile immunocompetent individuals presenting with non-specific symptoms in summers even in non-endemic areas should be considered. Because of the significant risk of mortality and morbidity of WNV future research should focus on double-blind prospective clinical trials to assess the efficacy of ribavirin, human intravenous immunoglobulin, and interferon-alpha in the treatment of neuroinvasive disease. Doing so may yield promising results for those affected by neuroinvasive WNV disease.

References


7. Centers for Disease Control and Prevention (CDC). West

<table>
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<tr>
<th>Author</th>
<th>Year</th>
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<th>Sex</th>
<th>Country</th>
<th>Presenting complaint</th>
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<td>Latif et al.</td>
<td>2018</td>
<td>35</td>
<td>Female</td>
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<td>Symptomatic management with intubation, airway protection, IVF</td>
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N/V, nausea/vomiting; IVF, intravenous fluids; NR, not reported.


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