West Nile Virus- A Neglected Tropical Disease of Arizona?

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INTRODUCTION

West Nile Virus (WNV) is a mosquito-borne flavivirus that was first reported in the United States in August 1999. Since its introduction to North America, WNV has caused an estimated 7 million cases of infection and is the leading cause of domestically acquired arboviral disease in the United States1. While most cases of WNV are subclinical or cause only mild symptoms, more severe infection presents as neuroinvasive disease causing meningitis, encephalitis, seizures, and/or acute faccial paralysis. Severe infection occurs in <1% of WNV cases, and advanced age is the most significant risk factor for the development of neurologic disease2.

The first confirmed case of WNV in Arizona occurred in 2003, and AZ typically experiences a biphasic WNV season with cases in early August and then late September3. Arizona experienced significantly higher average rainfall between the months of July and September 2021, which resulted in a larger mosquito population. In 2021, there were 472 confirmed and 1,095 suspected WNV cases in AZ- the highest amount ever recorded for the state. Of those cases, 65% (1,019) presented with encephalitis or meningitis4. In this report, we describe the case of an elderly patient with West Nile virus encephalitis.

LABS/IMAGING

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result</th>
<th>Normal Range</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>WBC</td>
<td>Day 1</td>
<td>6.7</td>
<td>Normal Range</td>
</tr>
<tr>
<td></td>
<td>Day 5</td>
<td>3.4</td>
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<tr>
<td></td>
<td></td>
<td>4.0-10.9</td>
<td>x 10^9/L</td>
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<tr>
<td>WNV Serum Antibody</td>
<td>Result</td>
<td>Ab not detected</td>
<td>Antibody detected</td>
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<tr>
<td>WNV Serum IgG</td>
<td></td>
<td>&lt;1.30</td>
<td></td>
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<tr>
<td>WNV Serum IgM</td>
<td></td>
<td>&gt;1.10</td>
<td>Antibody detected</td>
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<tr>
<td>Blood culture x2- no growth</td>
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CASE DESCRIPTION

History

A patient in their 7th decade of life with history of HTN, COPD, hypothyroidism, and aortic aneurysm presented for shortness of breath and fever. Patient had intermittent, worsening shortness of breath and confusion for 7 days and then developed fever 2 days prior to admission. Associated symptoms included nausea, diarrhea, and anorexia. Pertinent negatives included headache, chest pain, palpitations, abdominal pain, urinary difficulties, and lower leg edema. It was noted later that the patient had been gardening outside recently and likely experienced mosquito exposure. No sick contacts or travel were noted, and patient was not vaccinated against COVID-19. At baseline, patient was fully independent and still driving, but family member did note gradual memory loss for 3.5 years with no formal diagnosis of dementia.

Physical Exam

Vitals: T 99.1 F; HR 88, RR 18, BP 133/83, SpO2 94% on room air

General: Laying in bed, no acute distress, tremulous, slow to respond, no dysarthria

Cardiac: RRR, no murmurs, radial pulses 2+ bilaterally

Pulm: CTAB, no wheezes, no accessory muscle use

Skin/MSK: Warm, dry. Lower extremities without edema but mosquito bites scattered bilaterally

Neuro: A&O3, no focal deficits. CN II-XII intact. Strength +5/5 in all extremities. Negative Kernig and Brudzinski sign

Hospital Course

Day 1:
- Admitted and monitored overnight while preliminary workup initiated
- Bacterial or viral infection suspected, but etiology remained elusive as initial studies unremarkable

Day 2:
- Acute change in mental status with desaturation to 70% SpO2. Rapid Response and Stroke Alert called. O2 improved with jaw thrust and 6 L O2 via simple mask. ABG with pH 7.34/pCO2 44.2/pO2 101/HCO3 23.8 on 6 L O2 simple mask. ICU transfer did not occur during DNI status. Stabilized spontaneously without other interventions.
- Neurology and ID consulted. CT brain had no acute findings. Underwent LP with presumptive negative meningitis/encephalitis panel. Pulmonology consulted, recommended a nasal trumpet. Underlying COPD attributed to hypoxia/hypercapnia, also possibly confusion.

Day 3:
- Acute change in mental status with Rapid Response #2. Requirements O2 via NRB for SpO2 98-100%. Tachycardia RR 30s placed, on bipap. ABG with pH 7.27/pCO2 57.8/pO2 120/HCO3 26.7. Again, stabilized spontaneously.

Days 4-6:
- Respiratory status improved with fluctuating need for supplemental O2 0-3 L NC. By day 6, remained stable on room air. Concurrently, fever resolved, and confusion improved.

Day 7:
- A&O4 with mentation at baseline. Diagnosed with meningencephalitis of unknown etiology. WNV serology and CSF still pending. Discharged to SNF for continued recovery.

Post-discharge:
- WNV serology resulted

CULEX MOSQUITO

Culex mosquito species primarily involved in WNV transmission7

DISCUSSION

Arizona WNV cases during 2021 reached an all-time high due to heavy monsoon rains. Confirmed and probable WNV cases increased 801% in comparison to 2019, which was previously the year with the highest number of cases6. The majority (80-90%) of WNV cases are asymptomatic or subclinical2. Severe, neuroinvasive disease occurs in <1% of cases, and the elderly are most at risk for developing this5. Mortality from WNV neuroinvasive disease is approximately 12%5. In AZ, 110 deaths occurred in 2021, which was a 479% increase from 19 deaths in 20196.

This case demonstrates a classic presentation of neuroinvasive WNV in an elderly patient with comorbidities. WNV is a vector-borne virus transmitted primarily from mosquitoes to humans; transmission via breastfeeding, blood transfusion, and transplanting WNV-infected organs can also occur2. Incubation period ranges from 2-14 days5. This patient likely became infected with WNV while gardening several days prior to admission, resulting in encephalitis and episodes of acute flaccid paralysis associated with associated respiratory failure.

Laboratory diagnosis is typically made by testing serum and CSF for WNV IgM. It is important to note that WNV IgM antibodies develop 3-8 days after illness onset and can persist for 1 year or more after infection2. Serial studies of serum and CSF WNV IgM and IgG may be necessary to distinguish acute from past infection2. Treatment primarily consists of supportive care2. Frequency and severity of long-term sequelae remain unknown but can include movement disorders or cognitive problems2.

CONCLUSION

Once a novel pathogen, WNV is now endemic with significant clinical and economic implications in Arizona and throughout the US. Age-based vaccination is potentially the most effective method to combat WNV1. However, no vaccine currently exists, and no trials have passed phase II of preclinical research6. Due to the significant impact of severe WNV cases on the healthcare system and economy, more grant funding and research are needed both for a preventative vaccine for the elderly as well as effective therapeutic agents for acute neuroinvasive WNV5. In the interim, clinicians should consider and test for WNV in patients with fever and neurologic symptoms to help better calculate incidence and prevalence1. Prevention remains key via community-level mosquito control and household/personal measures to avoid mosquito bites6. Given that WNV may disproportionately affect vulnerable populations, occurs in climates conducive to mosquito-borne diseases, can be controlled by vector surveillance, and is inadequately addressed by both clinicians and policy makers, WNV can arguably be considered the next neglected Tropical Disease4.

REFERENCES

5. Peterson, L. Clinical manifestations and diagnosis of West Nile virus infection. UpToDate 2020.