West Nile Encephalitis and Poliomyelitis in a 12 Year Old

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Dr. Ashlesha Kaushik has documented no financial relationships to disclose or Conflicts of Interest (COIs) to resolve.
Assess the presentation, diagnosis and management of West Nile Virus infection in children
12 year old male with altered mental status
Mild cough, rhinorrhea x 5 days
Vomiting, fever and diarrhea x 2 days
Red rash in the form of small “spots”: disappeared at admission
Slurred speech and questionable generalized seizure activity progressing to right sided weakness and lethargy; altered sensorium.
Seen at outside hospital: Intubated, CT head and lumbar puncture; Transferred to PICU at Children’s.
**REVIEW OF SYSTEMS**

- **General:** fever
- **HEENT:** rhinorrhea, headache, no photophobia
- **CVS:** No Chest pain, palpitations, syncope
- **Respiratory:** cough, No dyspnea/wheezing
- **GI:** nausea, vomiting, diarrhea
- **GU:** No dysuria, frequency
- **Musculoskeletal:** no joint pain/swelling
- **Neurologic:** AMS, seizure
- **Hematologic:** No bleeding or easy bruising.
- **Skin:** rash
EXPOSURE HISTORY

- Had been camping at cousin’s house 1 week PTA (Palestine, Texas)
- Playing with dogs at home
- No swimming in lakes/pools: dogs were swimming in a “dog pond”
- No exposure to farm animals/cats.
- No intake of unpasteurized products.
- No known tick bites
- Immunizations: up to date
Vitals:
  Temp 39.5°C BP 122/50 mmHg
  Pulse 108/min RR 14/min  SpO2 99%
General: Intubated, sedated
Respiratory: Good air entry; no added sounds
Abdomen: No hepatosplenomegaly
Skin: No rash
NEUROLOGIC

- Deeply Comatose, NOT responsive to deep pressure/pain
- Questionable corneal reflexes; absent gag
- Pupils pinpoint, barely reactive
- Hypotonic
- DTRs: 2+ and symmetric
  - B/l plantar reflexes: equivocal on both sides.
- No involuntary movements
- No meningeal signs
Admitted to PICU

Started on vancomycin, cefotaxime, acyclovir and doxycycline

Consults: Infectious Diseases, Neurology

MRI: Cardiopulmonary arrest and seizure
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<tbody>
<tr>
<td><strong>WBC</strong></td>
<td>9.6</td>
<td>N 52/L36/ M11</td>
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<tr>
<td><strong>HGB</strong></td>
<td>13.8/38.9</td>
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<td><strong>PLT</strong></td>
<td>219</td>
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<td><strong>CHEMISTRY</strong></td>
<td>Sodium: 137</td>
<td>Potassium: 3.7</td>
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<td></td>
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<td>Chloride: 105</td>
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<td>CO2: 23</td>
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<td>BUN: 11</td>
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<td></td>
<td></td>
<td>Creatinine: 0.9</td>
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<td>LDH: 886</td>
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<td><strong>LIVER FUNCTION TESTS</strong></td>
<td>Alkaline Phosphatase 220</td>
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<tr>
<td></td>
<td>ALT: 19</td>
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<td>AST: 14</td>
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<td>Total Bilirubin: 0.40/ 0.10</td>
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<td>GGT: 16</td>
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### CSF

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<tr>
<td>Appearance</td>
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<tr>
<td>WBC</td>
<td>105 (S19/L52)</td>
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<tr>
<td>RBC</td>
<td>45</td>
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<tr>
<td>GLUCOSE</td>
<td>67</td>
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<tr>
<td>PROTEIN</td>
<td>86</td>
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<td>11/13</td>
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<td>Appearance</td>
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MRI FINDINGS
Edema of left thalamus, with a small focus of restricted diffusion on the DWI (diffusion weighted imaging) (MRI on Day# 2 of hospitalization)
Imaging

*Brain MRI* with T2 signal in the left thalamus and midbrain and subtle leptomeningeal enhancement on 11/15/2012: Seizure or encephalitis

Lab work negative EXCEPT.......
STUDIES: CSF: HSV PCR, Enterovirus PCR neg, NMDA receptor antibody Neg, gram stain/bacterial culture negative, Wright stain for amoebae negative, WNV PCR neg
Eastern equine, western equine, St. Louis, California encephalitis Ig M/IgG: Negative (CSF and serum)

SERUM: Ehrlichia serology (IgM and IgG), Rickettsial serology negative, Mycoplasma serology negative, HIV negative (serum)

OTHERS: Respiratory viral panel negative, Mycoplasma PCR (nasopharynx) negative
A week later

+West Nile IgM and IgG

ID and Neurology: IVIG X 5 days

Encephalopathy improved

Progression to West Nile Poliomyelitis

absent reflexes, flaccid quadriplegia
ENCEPHALITIS: DIFFERENTIAL DIAGNOSIS

-Viral:
- Arboviruses: WNV, St. Louis, dengue, La crosse, Eastern equine, western equine
- Novel viruses: Phleboviruses
- Adenovirus, HSV, enteroviruses, varicella, influenza

-Bacterial: Rickettsiae, Ehrlichia, Mycoplasma
-Amebic encephalitis
-Non-infectious causes: anti-NMDA antibody
Classified by cross-neutralization assays into 4 antigenic groups:

- **JE complex**: consisting of JE, St Louis, **WNV**, and Murray Valley encephalitis viruses;
- **Dengue complex**: 1 through 4 viruses;
- **Mammalian tick-borne virus complex**: Tick borne encephalitis (TBE), louping ill, Powassan, Kyasanur Forest disease, and Omsk hemorrhagic fever viruses;
- **Yellow fever virus**
WEST NILE VIRUS (WNV)

- Single stranded RNA flavivirus, first isolated in 1937 in a febrile patient in the West Nile district of Uganda
- Transmitted primarily through *Culex* mosquito bites
- Most of Africa, Asia, Australia, Europe, North America, and in some focal areas of Latin America and the Caribbean.
- First detected in New York City in 1999, the virus spread over the entire continental U.S.
CDC reported 5,387 cases of West Nile virus disease, including 243 deaths in 2012 (highest reported incidence since 2003)

Of these, 2,734 (51%) were classified as neuroinvasive disease and 2,653 (49%) were classified as non-neuroinvasive disease.

80% of cases from 13 states (Texas, California, Louisiana, Illinois, Mississippi, Michigan, South Dakota, Oklahoma, Nebraska, Colorado, Arizona, Ohio, and New York)

A third of all cases have been reported from Texas.
Mosquitoes become infected when they feed on infected birds (300 species)

Bird reservoirs will sustain an infectious viremia for 1 to 4 days after exposure after which the hosts that survive develop life-long immunity.

Particularly crows and jays
People, horses, and most other mammals are not known to commonly develop infectious-level viremias and thus are probably "dead-end" or incidental hosts.

- Summer/early fall
TRANSMISSION

West Nile Virus Transmission Cycle

- Mosquito vector
- Bird reservoir hosts
- Incidental infection (West Nile virus)
- Incidental infection (West Nile virus)

(CDC.GOV/WEST NILE VIRUS)
Mosquitoes that acquire WNV from birds *incidentally* infect humans.

In immunocompetent people, viremia usually lasts <7 days and viral concentrations in blood are too low to effectively infect mosquitoes.

Transfusion of infected blood and organ transplantation.

Rare: Transplacental transmission of WNV and breastfeeding.
Incubation period: 2 to 14 days

Majority are asymptomatic (80%)

20% develop West Nile fever: Abrupt onset of fever, headache, variably accompanied by abdominal pain, vomiting, diarrhea and a maculopapular rash.

Less than 1% develop WNND (West nile neuroinvasive disease):
- Meningitis (25-35%)
- Encephalitis (60-75%)
- Poliomyelitis (5-10%)
West Nile Poliomyelitis

- All age groups
- Can occur in isolation or in combination with meningitis or encephalitis
- Motor weakness is usually the result of a poliomyelitis-like process (pure motor deficit due to involvement of anterior horn cells), rather than a Guillain-Barré-like syndrome (motor and sensory deficit involving peripheral nerves)
- Worst prognosis
Fever
Gastrointestinal symptoms
Ataxia and extrapyramidal signs
Optic neuritis
Seizures
Weakness
Change in mental status
Myelitis; Polyradiculitis
A minority develop a maculopapular or morbilliform rash involving the neck, trunk, arms, or legs.
FEATURES OF SEVERE DISEASE

- Fever
- Gastrointestinal symptoms
- Ataxia and extrapyramidal signs
- Optic neuritis
- Seizures
- Weakness
- Change in mental status
- Myelitis; Polyradiculitis
- A minority develop a maculopapular or morbilliform rash involving the neck, trunk, arms, or legs.
Most efficient diagnostic method: IgM antibody to WNV in serum collected within 8 to 14 days of illness onset or CSF collected within 8 days of illness onset

CSF PCR only 50% sensitivity: a negative test does not rule out a WNV infection.

Significant increase in WNV-specific neutralizing antibody titer between acute- and convalescent-phase serum specimens confirms acute infection.

MRI usually normal; Signal abnormalities in thalamus, basal ganglia, brainstem, Spinal cord
COMPLICATIONS

- Chorioretinitis,
- Cardiac dysrhythmias,
- Myocarditis,
- Rhabdomyolysis,
- Optic neuritis, uveitis,
- Orchitis,
- Pancreatitis and hepatitis
Mortality following WNND in adults is over 10%

Case-fatality rate for WNND in children in the U.S. is <1%.

WN Fever: Most recover completely, however, fatigue, malaise weakness

WNND: neurologic sequelae; West Nile Poliomyelitis has worst prognosis, strength recovery usually within first 6-8 months with subsequent plateau
Supportive.

Ribavirin, and/or interferon have been given to patients with WNND with inconclusive results.

Anecdotal reports of improvement following administration of high-titer anti-WNV immunoglobulin, but evidence from clinical trials is lacking.
Protection against West Nile Virus Infection in Mice after Inoculation with Type I Interferon-Inducing RNA Transcripts

Alpha/beta interferon protects against lethal West Nile virus infection by restricting cellular tropism and enhancing neuronal survival. *J. Virol.* 2005

Mice lacking IFN-α/βR are highly vulnerable to WNV with 100% mortality within 4 days, even after infection with 1 plaque forming unit of virus

Effect of interferon-alpha and interferon-inducers on West Nile virus in mouse and hamster animal models *Antivir Chem Chemother.* 2004

Prophylaxis of rodents with IFN-α protects against lethal WNV infection
Using high titer West Nile intravenous immunoglobulin from selected Israeli donors for treatment of West Nile virus infection. *BMC Infec Dis.* 2009

WNIG was about 10 times more potent (per gr of IgG) than was regular IVIG-IL when tested by ELISA and neutralization assays. In a mouse lethal WNV infection model, prophylactic treatment with WNIG was at least 5-10-fold more potent as compared to treatment with IVIG-IL. Treatment with WNIG during active encephalitis, three or four days following WNV infection, had a significant protective effect. WNIG was also very effective in protecting immunosuppressed mice. Indeed, treatment of dexamethasone-immunosuppressed mice with 0.2 or 1.0 mg WNIG 4 h after virus infection, led to 100% survival.

Successful treatment with intravenous immunoglobulin of acute flaccid paralysis caused by west nile virus. *Perm J.* 2009
No available vaccine

Primary prevention step: **use of mosquito repellent when outdoors.** Mosquitoes may bite through thin clothing, so spraying clothes with repellent containing permethrin

- Wearing protective clothing when outdoors.
- Avoiding mosquitoes: Dusk to dawn
- Aerial sprays; removing standing water
- WNV encephalitis nationally notifiable
THANK YOU !!