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CLINICAL VIGNETTE

Arthralgias, Rash, Fevers, and Left Arm Weakness – A Case of West Nile Virus with Acute Flaccid Paralysis

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A 52-year-old Asian-American male with no significant past medical history presented to the emergency department in August with rash arthralgias, low grade fever, and left arm weakness. He had been in his usual state of health until ten days prior when he developed diffuse, bilateral joint pains that became migratory. He subsequently developed a rash involving the palms and soles as well as macular lesions involving the soft palate. He was seen by his primary care provider and was treated with naproxen for suspected Hand, Foot and Mouth disease. His rash ultimately spread to involve his entire body. He then noticed a tremor in his left hand as well as left upper extremity weakness. Four days prior to being seen in the ED, the rash was resolving, but he noted subjective fevers, generalized weakness, nausea and vomiting. On the day prior to arrival, he had multiple episodes of vertigo. Of note, he had recently traveled to Hawaii earlier in the month where he swam in the ocean but not freshwater. He denied any insect bites nor contact with wild animals. He reported one new sexual partner and did not use protection.

In the emergency department, the patient was afebrile with normal vital signs. Physical examination was notable for left upper extremity ataxia and 4/5 weakness with intact sensation. He had unsteady gait and positive Romberg. He had a faint, resolving maculopapular rash noted on the medial aspect of bilateral feet. Laboratory data revealed leukocytosis with white blood cell count of $14.6 \times 10^3/\mu\text{L}$ and elevated inflammatory markers including erythrocyte sedimentation rate of 48 mm/hr and C reactive protein level of 7.2 mg/dL. Lumbar puncture was performed and cerebrospinal fluid (CSF) was notable for a lymphocytic pleocytosis with elevated protein level and normal glucose. He underwent magnetic resonance imaging of his brain and cervical spine, both of which were unremarkable. Neurology and Infectious Disease consultations were requested.

The initial differential diagnosis for this patient was broad. The constellation of rash involving the palms and soles, arthralgias, and a new sexual partner raised concern for secondary syphilis. The differential for a rash that starts on the soles of feet and palms of hands includes Rickettsial disease such as Rocky Mountain Spotted Fever and hand, foot and mouth disease, although less likely in the absence of exposures. Fever, arthralgia, and left arm weakness in the setting of recent travel also raised the possibility of West Nile Virus (WNV) with possible early signs of acute flaccid paralysis. Other viral exanthems considered included enterovirus, EBV, HSV, CMV, Coxsackie and St. Louis encephalitis virus. Lyme disease

involving the central nervous system was also entertained. Antibody testing targeting the above infectious etiologies was done on the cerebrospinal fluid. WNV IgG and IgM both returned positive in the CSF confirming the diagnosis of WNV. The patient's hospital course was complicated by urinary retention requiring urinary catheterization. It was thought that the retention was likely WNV involvement in the lumbar spine. MRI of the lumbar spine was considered but deferred as it would not change management. Treatment for West Nile Virus is primarily supportive care. The patient underwent physical therapy and occupational therapy while inpatient and at an inpatient rehabilitation facility. He followed up with neurology two weeks after discharge and continues to have residual weakness in the left upper extremity, now primarily limited to the hand.

Discussion

West Nile virus (WNV) is a virus within the *Flaviviridae* family and *Flavivirus* genus. The virus is maintained in a bird-mosquito-bird transmission cycle and affects humans when they are bitten by an infected mosquito (typically of the *Culex* mosquito species).

WNV has become endemic in all 48 contiguous United States, although incidence varies widely among states. In California, the total number of WNV cases reported to the CDC from 1999-2016 total 6,031 (compared to 46,086 or 13% of total cases in the US). The total number of neuroinvasive WNV cases in California from 1999-2016 total 3,390 (compared to 21,574 or 15% of total cases in the US).¹ The incidence of the disease also varies by time of year with the majority of cases occurring between July and October.¹ Interestingly, West Nile virus is not endemic in Hawaii. Cases in Hawaii have been infected outside of Hawaii, although the mosquitoes competent to transmit these viruses are present and wide spread.²

The symptoms of WNV are typically sudden in onset and often include headache, malaise, fever, myalgia, chills, vomiting, rash, fatigue, and eye pain.³ Given that our patient's distinguishing symptoms were his rash and neurologic findings, we will discuss each in further detail.

Incidence of rash in WNV has been variable with case reports citing frequency anywhere from 14-60% of WNV cases. Additionally, the rash associated with WNV does not have a characteristic appearance or pattern of onset or spread that helps

distinguish it from other etiologies. A report from 15 patients during the WNV outbreak in Colorado (2003) described the majority of rashes as maculopapular (80%) with variable location of onset (43% trunk, 21% head or neck, 14% upper extremities, 7% lower extremities, 14% multiple sites) and subsequent spread (at some point the rash affected the trunk in 93%, upper extremities in 93%, lower extremities 80%, and head or neck in 53%). One patient described palmar and oral lesions; one patient described palmar lesions alone.⁴

Neurologic symptoms are rarer, affecting <1% of WNV cases (although there is a higher incidence in patients who come to medical attention and/or are reported to the CDC). Neuro-invasive WNV can be categorized as 1) meningitis; 2) encephalitis; and 3) acute flaccid paralysis where acute flaccid paralysis is characterized by acute onset of limb weakness with at least 2 of the following: asymmetry, areflexia/hyporeflexia, abscess of pain/paresthesias, CSF pleocytosis and elevated protein, electrodiagnostic showing anterior horn process, or MRI findings of abnormally increased signal in anterior grey matter.⁵ Other common neurologic findings include extrapyramidal symptoms such as tremors, myoclonus, or Parkinson's.⁵

A study of 219 cases of neuroinvasive WNV disease during the Colorado outbreak (2003), identified 32 patients with acute flaccid paralysis characterized by acute limb weakness. Twenty six (81%) had concomitant meningitis and/or encephalopathy while 6 (19%) had paralysis alone. Of those 27 (84%) had poliomyelitis-like syndrome, 4 (13%) had Guillain-Barre syndrome, and 1 (3%) had a brachial plexus neuropathy of the long thoracic nerve. Poliomyelitis-like syndrome most frequently presents as tetraplegia or quadriplegia (asymmetric weakness in ≥ 3 limbs; n=16), but can also be characterized by acute monoplegia (n=5), asymmetric upper extremity weakness (n=1), or asymmetric lower extremity weakness (n=5). This is typically due to anterior horn involvement with or without motor axonopathy. Sensory impairment was rare (n=2), although preceding pain in associated limb was relatively common (n=16).⁶ Cranial nerves can also be involved and bowel/bladder dysfunction can be seen.⁵ While MRI can show lesions in the basal ganglia, thalami, brainstem, and/or anterior cord and ventral roots; over half of patients who received MRIs did not have any abnormal findings. Of note, 17 patients (53%; 11 with poliomyelitis-like syndrome and 1 with Guillain-Barre syndrome) had respiratory symptoms with evidence of diaphragmatic paralysis or neuromuscular respiratory failure. Of these, 12 patients required intubation. Respiratory failure was more common in immunocompromised patients and those with concomitant encephalitis. Lower bulbar symptoms such as dysarthria and dysphagia were predictors of respiratory failure. Unfortunately, while nearly all patients had improvement in their strength at the 4 month follow-up, all except 2 (both with Guillain-Barre syndrome) continued to demonstrate weakness.⁶

We suspect our patient acquired WNV in California (the recent trip to Hawaii being a red herring). He developed typical symptoms including headache, malaise, myalgias, fatigue. Although he did develop a generalized rash, his palmar and

plantar lesions seem atypical. Additionally, he developed neurologic symptoms consistent with acute flaccid paralysis involving the left upper extremity associated with bladder dysfunction without signs or symptoms of meningitis or encephalitis.

In summary, WNV should be considered in patients with acute viral illness, especially those with rash and/or neurologic findings. In addition to meningitis and encephalitis, acute flaccid paralysis is another possible manifestation of neuro-invasive WNV. Acute flaccid paralysis is most commonly characterized as a poliomyelitis-like syndrome with limb weakness and can be associated with respiratory failure.

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