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Single Case – General Neurology

Symmetric Ascending Paralysis Secondary to West Nile Virus

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Abstract
West Nile virus (WNV) is classified as a *Flavivirus*, belonging to a Japanese encephalitis subgroup often transmitted via mosquitoes. The classic presentation of a WNV infection usually displays high fevers, myalgias, and headache which can progress to neck stiffness, stupor, and coma (Case Rep Infect Dis. 2020;2020:6501658). Our case study presented with a rare manifestation of ascending paralysis, encompassing the feared neuroinvasive disease pattern that is seldom exhibited. This case had an unusual presentation as certain manifestations experienced by our patient closely resembled that of Guillain-Barré syndrome, although others were more indicative of poliomyelitis-like syndrome. Overall, the mainstay of therapy in both conditions is supportive care, although the prognosis varies substantially depending on the underlying diagnosis.

Introduction

West Nile virus (WNV) is classified as a *Flavivirus*, belonging to a Japanese encephalitis subgroup often transmitted via mosquitoes. The natural reservoir hosts are birds which allow the virus to perpetuate in a mosquito-bird-mosquito cycle [2]. The incidence of the virus peaks during the late summer and early fall. Once a person is inoculated, there is an incubation period that ranges from 3 days to 3 weeks [3]. Symptomatology of those infected with WNV usually consists of constitutional symptoms including fever, myalgia, headache, nausea, vomiting, and rash. Unfortunately, in rare instances, the virus can cause neuroinvasive disease, resulting in muscle weakness, altered mental status, seizures, and flaccid paralysis.

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Patients with neuroinvasive disease often present with clinical manifestations resembling rapidly progressing encephalitis, leading to flaccid paralysis, mirroring that of Guillain-Barré syndrome (GBS) or poliomyelitis-like syndrome [4]. The incidence of WNV with neuroinvasive disease has been described as 4.3/100,000 and occurs in approximately 1:150 of WNV cases [5]. Poliomyelitis-like syndrome is the more common of the two presentations, although GBS secondary to WNV has also been described in the literature. Distinguishing between the two syndromes typically requires a thorough history including timing of symptoms, physical exam, cerebrospinal fluid analysis, imaging and neurologic/electrodiagnostic testing. There is limited evidence supporting the use of intravenous immunoglobulins (IVIG) and plasmapheresis early in the course of GBS, although supportive care remains the mainstay of treatment for both conditions [6]. Distinguishing between the two syndromes provides useful insight in regards to long-term prognosis.

Case Presentation

A 67-year-old male with a history of coronary artery disease and hyperlipidemia originally presented to the emergency room with complaints of fever, nausea, vomiting, and right lower quadrant abdominal pain that began 1 week prior. He denied any sick contacts but did travel to a lake in the North Carolina mountains a few weeks prior to presentation. He was vaccinated against COVID-19 and found negative upon testing. He was febrile with a temperature of 39.2°C, although labs were unremarkable without evidence of leukocytosis. A CT of the abdomen and pelvis with contrast showed evidence of diverticulosis but no acute findings. Portable chest X-ray and electrocardiogram were unremarkable. Blood cultures were drawn. He was initially diagnosed with viral gastroenteritis, but before further work up or treatment, the patient decided that he wanted to go home and refused admission.

The following morning, his wife reported that he could barely stand up due to extreme weakness and was experiencing new-onset confusion along with persistent fever. Due to progression of symptoms, the patient again reported to the emergency department. Upon repeat presentation, he was afebrile and hemodynamically stable. On physical exam, the patient was alert and oriented to person, place, and time; had labored respirations and 4 out of 5 muscle strength in the bilateral lower extremities; and deep tendon reflexes were intact. His labs now showed elevated liver function tests (ALT/AST 83 IU/L and 87 IU/L, respectively), an elevated lactic acid of 2.3 mmol/L, and a procalcitonin of 0.22 ng/mL. Urinalysis was unremarkable for infection. A repeat portable chest X-ray showed the lungs to be underexpanded with left upper lobe atelectasis versus infiltrate. A CT of the head without contrast showed atrophy but no acute changes. An abdominal ultrasound showed hepatic steatosis with mild splenomegaly. Blood cultures, sputum culture, urine culture, and a methicillin-resistant *Staphylococcus aureus* nasal screen culture were sent. With concern for community-acquired pneumonia in the emergency department, he was started on ceftriaxone and azithromycin and admitted to the hospital.

The following day, infectious disease was consulted. Due to concern for meningitis versus encephalitis, vancomycin and acyclovir were added to the antibiotic regimen in addition to ordering an MRI of the brain. The MRI was read as normal with some mild sinus disease. Neurology was consulted and noted the patient to be extremely encephalopathic. His exam was significant for orientation only to self, adequate eye tracking, 1 out of 5 strength bilaterally in the lower extremities, diminished reflexes in bilateral lower extremities, 3 out of 5 strength in the bilateral upper extremities, and mumbling with incoherent speech. Nursing staff also noted new-onset bowel and bladder incontinence. Neurology recommended an MRI of the cervical, thoracic, and lumbar spine with and without contrast, electromyography,

and lumbar puncture. The MRI of the cervical spine revealed stenosis but no acute pathology. The MRI of the thoracic spine showed no acute disease processes with a normal central canal and intervertebral neuroforamina. The MRI of the lumbar spine showed multilevel spinal stenosis without evidence of acute fracture or other significant pathology. After further discussion with radiology, no significant findings were noted in the anterior spinal cord, indicative of damage to anterior horn cells. The lumbar puncture showed WBC 98/mm^3, protein 168 mg/dL, glucose 49 mg/dL, and albumin 108.0 mg/dL. Cultures were negative. Antibodies to WNV, *Borrelia burgdorferi*, Eastern equine encephalitis, HIV, and a paraneoplastic encephalitis antibody panel were sent for testing. EMG revealed nonrecordable nerve conduction velocity in the right and left peroneal nerve to the popliteal fossa, normal left tibial nerve conduction velocity with a slowing of the right tibial nerve conduction velocity consistent with neuropathy. No evidence of sensory deficit was noted on EMG.

Later that day, he was found to have increased work of breathing with hypoxia, requiring supplemental oxygen via nasal cannula. Critical care was consulted for his tachypnea, and the patient was placed on bilevel positive airway pressure therapy. His negative inspiratory force was −10 cm of water, and the decision was made to intubate the patient for impending respiratory failure secondary to diaphragm weakness. Repeat MRI of the brain and lumbar spine with and without contrast were ordered which were unchanged from prior with no evidence of acute pathology. Antibody testing from prior lumbar puncture returned that afternoon and was positive for WNV antibodies and negative for all other pathogens tested. The paraneoplastic antibody panel later returned negative as well. Antibiotics were discontinued, and he received a 3-day course of IVIG as well as 1 g of methylprednisolone daily for a course of 5 days.

Overall, the patient spent 31 days in the intensive care unit and failed multiple extubation attempts. He eventually required a tracheostomy and a percutaneous endoscopic gastrostomy tube with discharge to a long-term care facility. After approximately 7 months, he was discharged home with some residual lower extremity weakness but no longer required tracheostomy or percutaneous endoscopic gastrostomy tube feeding. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000529120).

Discussion

WNV is an enveloped, single-stranded RNA virus that is a member of the Flaviviridae family [1]. It is an arbovirus that is transmitted to humans most often via a mosquito bite. West Nile infection can cause a wide variety of presentations, ranging from asymptomatic infection, fever, and myalgias, to rapidly progressing neuroinvasive disease with flaccid paralysis often secondary to encephalitis [7]. Statistically, most patients infected with WNV remain asymptomatic, although 25% develop fever and less than 1% develop neuroinvasive disease [8].

Neuroinvasive disease is rare with an estimated incidence of 4.3/100,000. Poliomyelitis-like syndrome is the most common presentation of neuroinvasive disease with an estimated incidence of 3.7/100,000 [9]. The exact mechanism of central nervous system infection remains unclear, but multiple theories exist including a direct crossing of the blood-brain barrier by viral specimens, passive transport through the post endothelium, macrophages containing the infectious viral particles facilitating the transport across the blood-brain barrier, or potential direct axonal retrograde transport of viral particles. It is believed that once the virus gains access to the central nervous system, it induces an inflammatory response resulting in loss of neurons throughout the spinal cord and brainstem [8].

The flaccid paralysis associated with neuroinvasive disease typically presents as either GBS or poliomyelitis-like syndrome also known as WNV-associated acute flaccid paralysis. Distinguishing between the two syndromes is often difficult as there are overlapping aspects. The distinction is often based on symptomatology, CSF analysis, and electrodiagnostic testing. Distinguishing between the two syndromes is critical as there is a vast difference in therapy and overall prognosis. If recognized early, both plasmapheresis and IVIG have been reported as effective therapies in reducing overall morbidity and mortality in GBS [10]. Unfortunately, no effective treatment strategies have been identified for poliomyelitis-like syndrome secondary to WNV, and supportive care remains the mainstay of therapy [11]. It is estimated that 70% of patients with GBS experience a full recovery with gradual improvement over a span of weeks to years [12]. This differs from those diagnosed with poliomyelitis-like syndrome which often results in permanent deficits as damage to the anterior horn cells of the spinal cord is believed to be irreversible [13].

GBS occurs due to an inflammatory response toward peripheral nerves, usually secondary to an underlying infection [14]. The exact pathogenesis is not fully understood, although patients diagnosed with GBS have been found to have antibodies against gangliosides in peripheral nerves [15]. Clinical manifestations of GBS include symmetrical weakness beginning 1–2 weeks after the onset of acute infection, the absence of fever and leukocytosis, sensory loss, and pain. GBS rarely presents with encephalopathy or bowel and bladder involvement. There are no diagnostic radiologic findings in GBS, but imaging can help differentiate GBS from alternative diagnosis [16]. Nonspecific findings on MRI can include thickening and enhancement of anterior spinal nerve roots [17]. Lumbar puncture with CSF analysis is essential with the hallmark finding of elevated protein in the absence of pleocytosis known as albuminocytologic dissociation [16]. Despite high specificity, albuminocytologic dissociation is not present in 10% of cases [18]. Electrodiagnostic studies typically reveals symmetrically reduced compound muscle action potentials, reduced sensory nerve action potentials known as sensorimotor polyneuropathy, and demyelination [16]. Criteria have been proposed to assist clinicians in determining the likelihood of GBS based on electrodiagnostic findings. Included in these criteria, two nerves must have a conduction velocity of less than 70% of the lower limit of normal or a distal motor latency of greater than 150% of the upper limit of normal [19]. If recognized early, within 2 weeks of onset, plasmapheresis and IVIG can provide effective therapy. To date, steroids have not shown to provide treatment benefit in GBS [10].

Poliomyelitis-like syndrome secondary to WNV causes extensive damage to anterior horn cells, resulting in denervation of muscles. Manifestations of poliomyelitis-like syndrome include acute onset of asymmetrical weakness, fever, leukocytosis, and lack of sensory involvement. Unlike GBS, encephalitis and bowel/bladder involvement is common. Symptoms typically begin within days of initial infection [16]. Similar to GBS, there are no pathognomonic radiologic findings in poliomyelitis-like syndrome, although MRI may reveal hyperintensities along the anterior horns of the spinal column [11]. CSF analysis often reveals pleocytosis with elevated protein count. Electrodiagnostic studies exhibit asymmetrically reduced/absent compound muscle action potentials, preserved sensory nerve action potentials, axonal degeneration, and widespread asymmetric denervation without evidence of demyelination [16]. Unfortunately, no effective therapy has been identified, and the deficits are often irreversible.

In this case, the viral infection presented as a symmetric ascending paralysis, initially causing lower extremity weakness that progressed to acute hypercapnic respiratory distress, secondary to diaphragmatic paralysis. The patient had bowel and bladder incontinence and diminished deep tendon reflexes bilaterally, but sensation in the bilateral lower extremities was spared. The CSF cytology showed pleocytosis with elevated protein, and EMG showed symmetric reduction of nerve conduction velocity in the bilateral peroneal nerves to the

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popliteal fossa with sensory sparing. This was a rather atypical presentation with features of both GBS and poliomyelitis-like syndrome. The delayed onset of weakness occurring over a week after the onset of constitutional symptoms along with symmetric flaccid paralysis was consistent with GBS. On the other hand, bowel and bladder involvement, lack of sensory involvement, and the CSF fluid profile favor poliomyelitis-like syndrome. The EMG in our patient was indeterminant as it showed a reduction in compound muscle action potentials without sensory deficit consistent with poliomyelitis-like syndrome, although the findings were of symmetrical distribution. The symmetrical distribution is a rare finding overall but is more symbolic of GBS. One study reviewing 219 cases of neuroinvasive West Nile viral disease only found 4 patients exhibiting symmetric ascending paralysis [9]. The manifestations seen in our patient favored a poliomyelitis-like syndrome, although GBS could not be ruled out.

Conclusion

The goal of this case report is to encourage the inclusion of WNV in the differential in atypical presentations of infections that lead to ascending paralysis. West Nile infection can present with a wide array of symptomatology, ranging from asymptomatic infection to fever and myalgias to rapidly progressing neuroinvasive disease and even death. Diagnosis remains heavily dependent on good history taking and clinical suspicion, which in turn leads to the ordering of proper viral panels as imaging is often nonspecific and not directly indicative of viral etiology. In our case, the patient presented with nonspecific constitutional symptoms progressing to a symmetric ascending paralysis which eventually led to acute hypercapnic respiratory failure. Ascending paralysis in WNV is often secondary to either poliomyelitis-like syndrome or GBS. Symptomatology, cytology, and neurodiagnostic testing can assist in the distinction between the two syndromes which can provide insight into the overall prognosis. Poliomyelitis-like syndrome often results in irreversible damage, whereas an estimated 70% of patients with GBS experience a full recovery. There is limited evidence supporting the use of IVIG and plasmapheresis early in the course of GBS, although supportive care remains the mainstay of treatment for both conditions [6].

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

A.A. served as the corresponding author of the manuscript. N.S. served as a co-author of the manuscript. J.V. served as a co-author of the manuscript in addition to providing expertise in pulmonary and critical care. M.R. served as a co-author of the manuscript in addition to providing expertise in infectious disease

Data Availability Statement

All data that support the findings of this study are included in this article. Further inquiries can be directed to the corresponding author.

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