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Permalink

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Journal

Journal of Intensive Care Medicine, 31(4)

ISSN

0885-0666

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Publication Date

2016-05-01

DOI

10.1177/0885066615589734

Peer reviewed

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Journal of Intensive Care Medicine
1-3
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DOI: 10.1177/0885066615589734
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West Nile Meningoencephalitis Presenting as Isolated Bulbar Palsy With Hypercapnic Respiratory Failure: Case Report and Literature Review

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Abstract

Background: Since the outbreak of West Nile virus (WNV) in the United States in 1999, the WNV neuroinvasive disease has been increasingly reported with a wide spectrum of neuromuscular manifestations. **Case:** We submit a case of a 46-year-old male with a history of alcohol abuse, diabetes, hypertension, and hepatitis C who presented with fever, nausea, shortness of breath, and dysphagia. The patient rapidly developed hypercapnic respiratory failure and was found to have WNV meningoencephalitis without obvious neuromuscular weakness. His hospital course was significant for repeated failures of extubation secondary to persistent bulbar weakness eventually requiring tracheotomy. **Conclusion:** This is a unique case of WNV meningoencephalitis with bulbar palsy without other neuromuscular manifestations resulting in recurrent hypercapnic respiratory failure.

Keywords

West Nile virus, bulbar palsy, neuromuscular weakness, respiratory failure

Introduction

The incidence of West Nile virus (WNV) neuroinvasive disease in the United States has been rising, and there have been 3 large outbreaks since 2002. The WNV neuroinvasive disease often presents as a combination of meningitis, encephalitis, and neuromuscular disease. Common neuromuscular manifestations include a poliomyelitis-like acute flaccid paralysis, absent deep tendon reflexes, and respiratory failure. Respiratory failure and the inability to liberate from ventilatory support are often a result of diaphragmatic paralysis and generalized muscle weakness. Bulbar weakness presenting with dysarthria, dysphagia, and stridor secondary to pharyngeal laxity has been observed and often results in respiratory failure as well.[1] To our knowledge, isolated bulbar weakness as the solitary neuromuscular deficit in WNV infection has not been reported.

Case Presentation

A 46-year-old man with a history of alcohol abuse, hypertension, hepatitis C, and diabetes mellitus was brought to the emergency department for shortness of breath and tremors. His family noted that he usually drank 4 to 6 beers/day but had not been drinking for 1 week due to nausea, dysarthria, and dysphagia. On physical examination, the patient had a fever of 39.5°C, heart rate of 98, and an oxygen saturation of 97% on room air. He was confused and uncooperative. Lung examination was significant for diffuse bilateral rhonchi. Neurologic examination was without tremor, asterixis, or obvious focal motor deficits, and deep tendon reflexes were intact. Laboratory studies showed a white blood cell (WBC) count of 14 300/uL and a differential showing 78% neutrophils. Urine toxicology screen was positive for benzodiazepines, which had been administered in the emergency department prior to specimen acquisition. The patient was admitted to our step-down unit for suspected alcohol withdrawal; however, he rapidly developed hypercapnic respiratory failure—arterial blood gas upon admission to the step-down units was notable for pH 6.87, $PaCO_2$ 164 mm Hg, and PaO_2 50 mm Hg. During endotracheal intubation, which did not require neuromuscular blockade, direct laryngoscopy revealed

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Received March 26, 2015, and in revised form May 05, 2015. Accepted for publication May 11, 2015.

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laxity of the pharyngeal airway. Repeat arterial blood gas after initiation of mechanical ventilation showed a normalized pH, PaO_2, and $PaCO_2$. Chest radiograph was unremarkable. Liver function tests, including prothrombin time and serum albumin level, were within normal limits. Cerebrospinal fluid (CSF) analysis was significant for 345 WBC/μL with 96% lymphocytes, protein 124 mg/dL, and no organisms were seen on Gram stain or culture. The WNV immunoglobulin (Ig) G and IgM were positive in both the serum (1.70 and 5.6, respectively) and the CSF (1.67 and 6.02, respectively). Other bacterial, viral, and fungal studies were negative. Computed tomography and magnetic resonance imaging of the brain were unremarkable. The patient remained intubated for 6 days with altered mental status, copious secretions, and several failed spontaneous breathing trials. He was treated supportively with improvement in mental status and spontaneous respiration.

Prior to extubation, the patient was awake and following commands. His rapid shallow breathing index on a spontaneous breathing trial with pressure support level of 0 cm H_2O and a positive end-expiratory pressure of 0 cm H_2O was 80 breaths/min/L. Additionally, maximal inspiratory pressure was noted to be negative 43 cm H_2O. Immediately following extubation, the patient developed stridor with associated paradoxical abdominal movement and was reintubated for impending respiratory failure. Laryngoscopy, once again, revealed marked laxity and flaccid tone of the larynx. Tracheostomy was consequently performed, and he was gradually liberated from mechanical ventilation. The patient required frequent oral suctioning of retained secretions, and swallow evaluation revealed decreased oropharyngeal strength and absent initiation of pharyngeal swallowing. His voice was notably hypophonic necessitating communication through writing. A gastrostomy tube was placed for long-term nutritional support. At no point did the patient display other neurologic deficits and he exhibited full strength and mobility with physical therapy. However, he continued to have persistent isolated bulbar weakness requiring long-term tracheostomy and gastrostomy tubes and was discharged to a subacute rehabilitation facility for continued pulmonary hygiene. Prior to discharge, the patient was able to phonate with the use of a Passy-Muir speaking valve. Three months after discharge, the tracheostomy tube was removed, but the patient continued to have residual dysarthria and dysphagia requiring gastrostomy tube feeding.

Discussion

Since its entry into North America in New York City in 1999, reports of severe neurologic illness are becoming more frequent in confirmed cases of WNV.[1,2] West Nile virus is now endemic in all 48 of the contiguous United States with an incidence of approximately 2500 persons infected in 2013.[2,3] Among those infected, an estimated 60% to 80% of patients have a subclinical illness.[4] Symptomatic cases present with West Nile fever, which starts with flu-like symptoms including headache, malaise, myalgias, nausea, and occasionally morbilliform or maculopapular rash[1] after a 2 to 14-day incubation period.[1,2]

Table 1. Reported Spectrum of West Nile Disease.

Disease	Characteristics
West Nile fever	Headache, weakness, low grade fever, myalgia, morbilliform, or maculopapular rash
Meningitis	Nuchal rigidity, Kernig or Brudzinski sign, photophobia, or phonophobia
Encephalitis	Altered level of consciousness from confusional state to coma, tremor
Poliomyelitis	Selective anterior horn involvement resulting in acute flaccid paralysis. Can present as asymmetric monoplegia to quadriplegia
Transverse myelitis	Spinal sensory and motor deficits; sympathetic ganglia involvement causing autonomic instability
Myeloradiculitis	Spinal nerve root inflammation that can contribute to acute flaccid paralysis
Peripheral nerve involvement	Association with Guillan-Barré syndrome, myasthenia gravis, and brachial plexopathy

Neuroinvasive disease has been reported to occur in less than 1% of symptomatic infections; however, severe neurologic illness is being reported with greater frequency and is associated with increased mortality and morbidity.[2] Per 2014 data reported by the Centers for Disease Control and Prevention, as the number of cases with WNV disease has continued to increase in the central and western United States, there has been a concomitant increase in the incidence of neuroinvasive disease as well. The states with the highest incidences of WNV neuroinvasive disease were California, Arizona, North Dakota, South Dakota, Nebraska, and Louisiana. California reported the most cases of WNV neuroinvasive (536) and nonneuroinvasive (251) disease in the United States in 2014. Risk factors for development of neuroinvasive disease are poorly defined, but advanced age, diabetes, alcohol abuse, and immunosuppression have been implicated.[5,6] Any part of the nervous system can be affected resulting in a wide, overlapping clinical spectrum of syndromes of which meningitis, encephalitis, and acute flaccid paralysis are the most prominent (Table 1).[1,7] Signs and symptoms typical of viral meningitides, such as fever, headache, photophobia, and meningeal signs, characterize West Nile meningitis. Manifestations of encephalitis range from mild confusion to coma. A course bilateral tremor is often present with the encephalopathy and may be postural with a kinetic component.[8]

Neuromuscular complications are also prominent features of WNV neuroinvasive disease with studies reporting weakness as a clinical manifestation in approximately 50% of cases of WNV meningitis or encephalitits.[2,9,10] The most common neuromuscular presentation is a poliomyelitis-like syndrome with the destruction of the anterior horn cells of the spinal cord resulting in acute flaccid paralysis and absent deep tendon reflexes in affected limbs. Respiratory failure may occur as a result of weakness or paralysis of the diaphragmatic, intercostal, or bulbar muscles.[7] Other less common causes of weakness in WNV disease include inflammation of skeletal and cardiac muscles, motor axons, peripheral nerves, and the brachial plexus. When sympathetic neurons and ganglia are affected, patients may demonstrate autonomic instability.[2]

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Despite its rising incidence, the pathogenesis of neuroinvasion by WNV and the varied distribution of neuronal involvement are still not well understood. Neuroinvasive potential and phenotype have been associated with the viral genotype affecting viral structural proteins that possibly enhance binding and penetration of endothelial cells of the central nervous system.[10,11] Additional proposed mechanisms for neuroinvasion include breakdown of the blood–brain barrier from vasoactive cytokine and matrix metalloproteinase degradation, spread from the olfactory bulb, viral transport to the central nervous system through infected immune cells, and direct axonal retrograde transport from infected peripheral nerves. The host's innate immune system also plays a large role in reducing viral replication, preventing neuroinvasion, and reducing neuronal injury. Human genetic factors also influence the severity of WNV disease.[12]

Respiratory failure requiring endotracheal intubation and subsequent tracheostomy has been described with West Nile virus. An immunocompromised state and encephalitis are associated with an increased risk of intubation. Diaphragmatic and intercostal muscle paralysis is a common cause of respiratory failure.[2] Generalized weakness or flaccid paralysis leading to bulbar weakness has also been associated with respiratory failure in WNV neuroinvasive disease. Although the precise frequency of respiratory failure with WNV neuroinvasive disease is incompletely understood, one large observational study of patients with acute flaccid paralysis reported a 38% incidence of intubation and eventual tracheostomy.[13] Acute flaccid paralysis is typically symmetrical and rapidly progressive, reaching nadir weakness and potential respiratory failure within 2 to 8 days of symptom onset.[14] Bulbar symptoms arise from lower motor neuron injury to cranial nerves IX, X, XI, and XII in the medulla oblongata and pons. Injury to these nerves usually causes symptoms of dysarthria and dysphagia. Additionally, pharyngeal laxity can cause stridor.

Most patients with uncomplicated West Nile fever or meningitis have full recovery with supportive treatment. Some studies have reported fatigue, somatic, and cognitive symptoms lasting years after the initial illness. Approximately 10% of neuroinvasive disease cases are fatal. Patients with encephalitis resulting from WNV have increased morbidity and mortality as well as a prolonged course of symptoms compared to patients who develop meningitis alone. Patients with neuromuscular complications often report incomplete resolution of symptoms for up to 6 months to a year. Some of these patients only have partial recovery.[13] The duration of symptoms and the recovery period is variable and may not correlate with the severity of the initial illness.[1,2]

In this case of WNV meningoencephalitis, our patient presented with rapidly progressive bulbar weakness leading to profound hypercapnic respiratory failure. Radiologic and neurologic examinations during the acute neuroinvasive illness were otherwise normal, suggesting isolated lower motor neuron injury of cranial nerves. The patient's alcohol abuse and diabetes likely contributed to his susceptibility to neuroinvasive disease; however, it is unclear why the lower cranial nerves were most affected by the virus. Acute bulbar flaccid paralysis without other neuromuscular deficits caused by WNV infection has not been previously described; however, in the appropriate setting, it should be considered in patients with unexplained hypercapnic respiratory failure.

Authors' Note

Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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