

The Zika Virus: An Association to Guillain-Barré Syndrome in the United States - A Case Report

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Case of a 37 year-old Puerto Rican male with no past medical history who was admitted to the hospital after developing paresthesia in the upper and lower extremities with associated skin rash, weakness, and dysautonomia. After rigorous analysis of the clinical patterns, neurologic manifestations, laboratory workups, CSF analysis, and nerve conduction studies we conclude the existence of a strong relationship between the Zika virus and the Guillain-Barré syndrome. The patient recovered promptly and his response to treatment was excellent. [P R Health Sci J 2018;37(Special Issue):S93-S95]

Key words: ZIKA, Guillain-Barré, Zika and Guillain-Barré

The Zika virus is a flavivirus transmitted by vector-borne mosquitoes that has posed a serious threat to the global community. Multiple neurologic and congenital sequels have been reported in association with this virus (1,2,3).

We present one of the first reported cases of Guillain-Barré Syndrome associated with a locally acquired Zika virus infection in the United States in a patient that recovered promptly and whose response to treatment was excellent. As a differentiating factor from the predominant presentation in previously published series, our patient had a demyelinating subtype (Acute inflammatory Demyelinating Polyneuropathy) of the Guillain-Barré Syndrome.

This case underscores the need to become familiar with the features of the trending Guillain-Barré Syndrome associated with Zika virus.

Case Report

A 37 year-old Puerto Rican self-sufficient male with no past medical history was admitted to the University District Hospital on January 2016 after developing paresthesia in the upper and lower extremities with associated skin rash, weakness, and dysautonomia.

The patient had been well until thirteen days prior to admission when he first felt a “tingling” sensation in the hands with some “prickling” in the feet. He reports that two days after the onset of symptoms he developed a pruritic rash in the limbs that gradually extended to the trunk. He was treated with hydrocortisone and diphenhydramine at a neighborhood primary care clinic without significant improvement. Three days after the onset and while still experiencing the rash, he started noticing heaviness and weakness sensation in the legs. Four days later, the weakness progressed limiting his ability to walk and within one week the weakness was generalized in all four extremities. Subsequently, he developed high blood pressure,

blurry vision, dysarthria and dysphagia, which compelled him to seek medical attention at the University District Hospital of Puerto Rico.

Upon initial evaluation, the patient was alert and afebrile, mildly tachypneic (23bpm), tachycardic (120bpm) and with markedly elevated blood pressure (185/100mmhg) fitting the criteria for hypertensive urgency. Furthermore, the patient was unable to ambulate without maximal assistance; muscle strength was 4/5 proximally in both arms and legs, but 3/5 distally. There was bilateral weakness of the facial muscles, more conspicuous on the left side. Sensory examination revealed reduced vibratory sensation in the toes and fingers bilaterally, mildly decreased pinprick in the fingers and toes but with preserved proprioception. Patient’s deep tendon reflexes were absent in the upper and lower limbs and had plantar flexor response. Gait was not tested because of lower back pain. There was no visible rash or lymphadenopathy. Initial laboratory tests revealed leukocytosis, elevated hemoglobin and hematocrit, platelets within normal limits, mildly elevated erythrocyte sedimentation rate but normal C-reactive protein. Chest radiographs and magnetic resonance imaging of the brain performed without IV contrast showed no abnormalities. Toxicology, HIV-ELISA, along with blood, urine, and stool cultures were all negative. At all times, the patient maintained an adequate negative inspiratory force (NIF) of less than -40 cm H₂O.

In order to investigate our raised suspicion of demyelinating process versus CNS infection, a lumbar puncture was

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performed. Analysis of the cerebrospinal fluid specimen revealed a protein level of 288 mg per deciliter, a glucose concentration of 107 mg per deciliter (5.94 mmol per liter), with undetected white blood cells; results were remarkable for albumin-cytologic dissociation. Cerebrospinal fluid culture, cryptococcal antigen and gram stain were all negative. Nerve conduction studies and needle electromyography (EMG) were performed the day of admission and repeated 6 days after the initial study. The studies were significant for markedly prolonged distal latencies in the median, ulnar, peroneal and tibial nerves with mild to moderately reduced motor amplitudes and absent sensory responses (Table 1). Needle EMG in the left upper and both lower extremities showed decreased recruitment in proximal muscles with no signs of denervation. Neuromuscular studies were consistent of an acute demyelinating polyneuropathy evidenced with motor nerves of upper and lower extremity showing prolonged latency, diminished amplitude, mild decrease in conduction velocity and absent sensory responses.

A serum specimen collected one day after admission (15 days after onset of symptoms) was positive for the presence of anti-ZIKA IgM antibodies. The presence of Zika, Dengue and Chikungunya viruses were undetected by blood rRT-PCR. A urine specimen collected four days after admission was negative for detection of ZIKA nucleic acid by rRT-PCR.

One day after initial evaluation, the patient began intravenous immunoglobulins (IVIG) at 0.4g/kg with initial rate at 0.01g/kg/min titrated to a maximum rate of 0.08g/kg/min. Oxygen saturation was maintained above 95 percent with the use of a nasal cannula at a rate of 3 liters of oxygen/minute. Due to his fragile clinical presentation that included ascending paralysis, dyspnea and hypertensive urgency secondary to dysautonomia, the patient was transferred to the medical intensive care unit where immunoglobulin treatment was commenced.

After two successive days of IVIGs, the patient's neurological exam remained grossly unchanged. Vital signs stabilized with the exception of persistent sinus tachycardia. On the third day of IVIG administration, the patient demonstrated improvement in distal strength to 4/5 throughout bilateral upper and lower extremities and 5/5 strength in proximal lower extremity muscles. Patient stated resolution of his blurred vision and speech became more fluent. After completion of five days of IVIG, he reported improvement in mood, speech, and neurologic symptoms. On the sixth day, EMG was repeated and showed larger motor amplitudes and again absent acute or chronic denervation changes. After completing IVIG treatment, he was discharged to an inpatient rehabilitation facility and with outpatient Neurology follow-up.

Discussion

To the best of our knowledge, this case illustrates one of the first cases of Guillain-Barré Syndrome associated with a locally acquired Zika virus infection in the United States and/or its territories. Interestingly and distinctive from the predominant neuromuscular disease in previously published series in the French Polynesia between October 2013 and April 2014 (4), our patient had the demyelinating subtype Acute inflammatory Demyelinating Polyneuropathy (AIDP) of Guillain-Barré Syndrome, which is known to be the most prevalent type in the United States and Western Countries. This variant is characterized by a destructive immunological response toward the peripheral nerve myelin. The earliest abnormalities seen on clinical EMG in patients with AIDP are prolonged or absent F waves (3). As seen in table 1, a constellation of findings including slowed motor conduction velocity, delayed latencies, low distal amplitudes, and prolongation of minimum F wave latency were observed. Our EMG

Table 1. Summary of nerve conduction studies

Emg and Ncs of left median nerve at day 1 and day 6						
Date of study	Nerve	Distal motor	Distal amp	Proximal amp latency	Conduction velocity	Minimal F wave latency
Day 1	(L) Median	20.8	1.1	0.9	44	
Day 6	(L) Median	24.4	3.2	2.6	42	133

Emg and Ncs of left ulnar nerve at day 1 and day 6							
Date of study	Nerve	Distal motor latency	Distal amp	Forearm amp	Above elbow amp	Conduction velocity	Minimal F wave latency
Day 1	(L) Ulnar	6.8	2.3	1.8		38.7	
Day 6	(L) Ulnar	7.2	4.0	3.6	2.3	53	54

Emg And Ncs of left peroneal nerve at day 1 and day 6								
Date of study	Nerve	Distal Motor latency	Distal amp	Fibular neck amp	Pop Foss amp	Conduction velocity	Conduction V.Fib head	Minimal F wave latency
Day 1	(L)Perone Al	11.8	1.0	1.0		33.2		
Day 6	(L)Perone Al	10.8	1.4	1.3	1.4	32	37	70.8

Emg and Ncs of left tibial nerve at day 1 and day 6						
Date of study	Nerve	Distal motor latency	Distal amp	Proximal amp	Conduction velocity	Minimal F wave latency
Day 1	(L)Tibial	10.2	2.0	1.7	31.9	
Day 6	(L)Tibial	11.2	2.1	1.7	35	90.9

Summary: A constellation of findings including slowed motor conduction velocity, delayed latencies, low distal amplitudes, and prolongation of minimum F wave latency were observed.

and NCS findings were analyzed and compared to normal reference values described in published journal articles (3,5,6). Electrophysiological values were consistent with Guillain-Barré AIDP subtype.

The diagnosis of Guillain Barré Syndrome (7) was made using the recently developed Brighton criteria which was created as a response to the close association to the swine flu vaccination campaign 2009-2010. Our patient fulfilled the proposed diagnostic criteria for Level 1 diagnostic certainty, making it an unequivocal GBS case (8).

Given the positive IgM test for Zika, we can conclude the presence of a recent exposure to the Zika Virus. Even though the initial RT-PCR test for Zika was negative, it does not preclude the viral infection and this test must be interpreted in the context of the clinical, epidemiological setting and travel history according to the CDC guidelines.

After rigorous analysis of the clinical presentation, neurologic findings, ancillary laboratory test, and electrophysiological testing, we can conclude the existence of a strong relationship between the Zika virus and the Guillain-Barré syndrome (9).

Conclusion

Recent outbreaks of the Zika virus could represent a serious threat to our society. Controlling the spread of this mosquito-transmitted infection requires a multidisciplinary approach able to integrate medicine, law, ethics and public health policy into aggressive efforts that might mitigate potential global impacts. Understanding the pathophysiology of this disease, reporting new cases and creating public awareness are of outmost importance in the process of tackling this epidemic in time. Certainly, the implications of the Zika virus far outreach average health concerns. Only through increased public awareness, quick legislative response and successful fulfilling of executive orders can we have a real chance to eradicate this disease.

Resumen

Un varón puertorriqueño de 37 años de edad sin antecedentes médicos ingresó en nuestro hospital después de desarrollar parestesia en las extremidades superiores e inferiores con erupción cutánea, debilidad muscular y disautonomía. Luego de analizar los hallazgos clínicos, manifestaciones neurológicas, exámenes de laboratorio, análisis del líquido cefalorraquídeo y estudios de conducción nerviosa, podemos concluir la existencia de una fuerte relación entre el virus Zika y el síndrome de Guillain-Barré.

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