ACUTE ZIKA INFECTION WITH CONCURRENT ONSET OF GUILLAIN-BARRÉ SYNDROME

Case report. A 47-year-old Tongan male returning to New Zealand after a 2-week holiday in Tonga presented with 3 days of progressive limb weakness, numbness, unsteady gait, and dyspnea. Two days before departing Tonga (6 days before neurologic symptoms), he developed leg swelling with erythematous and pustular lesions, which were treated with flucloxacillin. He had no medical history, was not taking regular medication, and had a 20 pack-year smoking history.

Examination findings included the following: afebrile, pulse 80 beats/min, blood pressure 150/90 mm Hg, respiration 20 breaths/min, and oxygen saturation 98% (air). Cardiovascular and abdominal examinations were unremarkable. Cranial nerves and eye movements were normal. Limbs were hypotonic with globally reduced power (4/5), areflexia, and absent plantar responses. Temperature and pain sensation were impaired in hands and feet. Proprioception and vibratory sensation were impaired in the feet. Romberg test was positive.

Full blood count, renal function, electrolytes, creatinine kinase, hemoglobin A1c, C-reactive protein, thyroid function, B12, and folate were normal. Liver enzymes were mildly elevated (ALP 122, GGT 251, and ALT 41 IU/L). Antinuclear antibody was 1:160. CSF showed albuminocytologic dissociation: protein 0.69 g/L (reference 0.15–0.45), white blood cells 2/μL, red blood cells 1/μL, and glucose 3.4 mmol/L (serum glucose 6.0). Spine MRI and chest x-ray were unremarkable. Normal cranial MRI excluded concurrent acute disseminated encephalomyelitis. Nerve conduction study on day 2 of admission revealed demyelinating, predominantly motor, polyneuropathy (table). Serum reverse transcription (RT)-PCR on day 3 after illness onset was negative for chikungunya and dengue RNA and positive for Zika RNA (subsequently negative on day 13). Dengue NS1 antigen (Platelia Dengue NS1; Bio-Rad, Hercules, CA) was negative. Immunoglobulin (lgM) antibodies (low level) and lgG antibodies (high level) against Zika (EUROIMMUN, Luebeck, Germany) and dengue (PanBio, Brisbane, Australia) were detected on day 3. CSF RT-PCR on day 5 was negative for all 3 viruses.

A diagnosis of Guillain-Barré syndrome (GBS) was made. Worsening respiratory function required ventilation support. Five days of Ig was given (0.4 g/kg/d). Serial quantitative neurologic examination showed a steady decline. He was then given 6 plasma exchanges beginning 5 days after the last dose of Ig, i.e., from day 10 of treatment. Respiratory status improved to not requiring mechanical ventilation by day 21. At day 33, when transferred to rehabilitation, he had persistent limb weakness with best power grade 3/5 and remained bedbound.

Discussion. This case illustrates rapid development of severe acute demyelinating polyneuropathy linked with Zika virus infection. The pustular leg spots were probably infected mosquito bites, although the erythematous skin lesions may have also been related to Zika infection. There are no case reports of Zika-related GBS in New Zealand. There are reports of GBS associated with Zika infection in French Polynesia, South Pacific islands, and South and Central America. It is noteworthy in our case that Zika was detected by PCR in the serum while his clinical status was worsening. RT-PCR for Zika is sensitive and detects viral RNA concentrations as low as 900 copies/mL with high specificity and no cross-reactivity to other flaviviruses including dengue, West Nile, and chikungunya. Although the underlying mechanism remains unclear, GBS has been associated with other flaviviruses (dengue,3 West Nile virus,4 etc.). In this case, we demonstrated no evidence of direct CNS infection (negative CSF Zika PCR and normal cranial MRI) but clear evidence of simultaneous systemic Zika infection contemporaneous with the appearance of GBS.

Serologic cross-reactivity between flaviviruses means that currently available IgM antibody assays cannot reliably distinguish between Zika and dengue. The PCR and serology results suggested that the patient had a likely secondary flavivirus infection—a recent Zika virus infection in the context of preexisting anti-dengue antibody.

Unlike recent GBS case reports from 2014 to 2016 with only positive Zika serology (IgM), our case is of particular interest because Zika virus was present in the serum at the same time that GBS was developing. This suggests either direct neural injury by Zika or
rapid cellular-mediated response to Zika “molecular mimicry” with cross-reactivity against peripheral nerve, rather than an Ig-mediated mechanism, which would usually show a latent period. Flaviviruses are neurotropic, but, neuroinvasion processes are not fully understood. Neuronal virus attachment factors for Zika in the peripheral nervous system may be similar to those for West Nile virus, which are at the sensory nerve endings.\(^6\) After entering the neuron, the virus may then utilize axonal transport to spread in retrograde and anterograde directions.\(^7\) These postulated mechanisms may in part explain rapidity of onset of Zika-associated GBS, but further study is needed because there are no definitive data.

From the Department of Neurology (R.S., W.B., P.T.), Waikato Hospital, Hamilton; and Arbovirus Reference Laboratory (A.T., W.G., Q.S.H.), Institute of Environmental Science and Research, Wellington, New Zealand.

Author contributions: Ronald Siu: drafted and edited the manuscript. Wajih Bukhari and Paul Timmings: reviewed and edited the manuscript. Angela Todd: performed real-time RT-PCR, interpreted the results, and critically reviewed the manuscript. Wendy Gunn: conducted serologic testing, interpreted the results, and critically reviewed the manuscript. Qiu Sue Huang: interpreted the results and critically reviewed the manuscript.

Study funding: No targeted funding reported.

Disclosure: The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

Received February 25, 2016. Accepted in final form June 28, 2016.

Correspondence to Dr. Siu: ronaldsiu@alumni.unimelb.edu.au or Dr. Timmings: paul.timmings@xtra.co.nz

© 2016 American Academy of Neurology


Acute Zika infection with concurrent onset of Guillain-Barré Syndrome
Ronald Siu, Wajih Bukhari, Angela Todd, et al.
Neurology published online July 27, 2016
DOI 10.1212/WNL.0000000000003038

This information is current as of July 27, 2016

Updated Information & Services
including high resolution figures, can be found at:
http://www.neurology.org/content/early/2016/07/27/WNL.0000000000003038.full.html

Citations
This article has been cited by 2 HighWire-hosted articles:
http://www.neurology.org/content/early/2016/07/27/WNL.0000000000003038.full.html##otherarticles

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
All clinical neurophysiology
http://www.neurology.org/cgi/collection/all_clinical_neurophysiology
All Infections
http://www.neurology.org/cgi/collection/all_infections
Guillain-Barre syndrome
http://www.neurology.org/cgi/collection/guillainbarre_syndrome
Peripheral neuropathy
http://www.neurology.org/cgi/collection/peripheral_neuropathy
Public health
http://www.neurology.org/cgi/collection/public_health
Viral infections
http://www.neurology.org/cgi/collection/viral_infections

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.neurology.org/misc/about.xhtml#permissions

Reprints
Information about ordering reprints can be found online:
http://www.neurology.org/misc/addir.xhtml#reprintsus

Neurology © is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2016 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.