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TROPICAL, TRAVEL AND EMERGING INFECTIONS (L. CHEN AND A. BOGGILD, SECTION EDITORS)

Zika Virus-Associated Aseptic Meningitis and Guillain–Barre Syndrome in a Traveler Returning from Latin America: a Case Report and Mini-Review

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Abstract
ZIKV-associated Guillain–Barré syndrome presents with an accelerated clinical course compared to classic post-infectious Guillain–Barré syndrome. Clinicians should anticipate and screen patients with ZIKV infection for neurologic complications bearing in mind that these may manifest during the acute viremic phase or during early convalescence.

Keywords Emerging infectious diseases · Flaviviruses · Guillain–Barre syndrome · Vector-borne infections · Zika virus

Introduction/Clinical Case

A 34-year-old Canadian-born woman traveled to Nicaragua for tourism in August 2016. On the tenth day of travel, she developed a papular rash across her chest that spread along her arms, legs, and face. She became febrile and complained of muscle fatigue and weakness involving her arms and legs, arthralgia of the wrists and ankles, and global headache with photophobia. Exposures during the trip were notable for several daytime mosquito bites. She had no prior travel history and had not received prior immunization against yellow fever. She was assessed by a physician in Nicaragua who made a presumptive diagnosis of Zika virus (ZIKV) infection but no diagnostic investigations were performed.

She returned home 4 days after the onset of symptoms and was assessed in our unit the following day. On physical examination, the patient was afebrile with normal vital signs, with a macular rash on the lower extremities, and tender non-effusive joints in the hands, wrists, elbows, and feet. Neurologic examination identified global weakness, most pronounced in the left hip flexor (4/5). Deep tendon reflexes were normal (2+) throughout. Sensation was intact but reduced in the left lower extremity. Routine blood work was normal with negative malaria testing. Serologies for travel-related infections were ordered (Table 1) and the patient was discharged home with instructions to rest and return before her 1-week follow-up should any symptoms worsen.

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Table 1 Summary of Investigations

Parameter	Result
Hemoglobin (g/L)	146
WBC (× 10^9/L)	6.9
Platelets (× 10^6/L)	228
Serum creatinine (μmol/L)	74
Serum glucose	4.6
AST (U/L), ALT (U/L), ALP (U/L)	45, 54, 47
Total bilirubin (μmol/L)	7
Beta HCG	Negative
CSF	
WBC (× 10^6/L)	28 (83% lymphocytes)
Protein (g/L)	0.49
Glucose (μmol/L)	3.3
HSV (PCR)	Negative
VZV (PCR)	Negative
WNV	Negative
ZIKV (PCR)	Detected
Serum virus detection	
ZIKV (PCR)	Not detected
Dengue virus (PCR)	Not detected
Chikungunya virus (PCR)	Not detected
Serology	
Zika virus	IgM positive ZIKV PRNT > 1:160, Dengue PRNT Negative
Dengue virus	IgM + IgG Non-reactive
Chikungunya virus	IgM + IgG Non-reactive
West Nile virus	IgM + IgG Non-reactive
Epstein–Barr virus	EBNA IgG negative; EBV VCA IgG positive
Cytomegalovirus	IgG non-reactive
Human immunodeficiency virus	Non-reactive

Four days later, she re-presented to our institution with headache, debilitating muscle weakness, and an inability to ambulate independently. On examination, she was afebrile and without rash. Neurologic examination revealed worsening lower extremity muscle weakness in the left hip flexor (3/5) and diminished power (4/5) in the rest of upper and lower extremity muscle groups. Deep tendon reflexes were diminished (1+) and symmetric in the upper and lower extremities. Sensory examination demonstrated decreased light touch, pain, and temperature sensation in a 'glove-and-stocking' distribution. Cranial nerve examination revealed decreased sensation (soft touch, pain, and temperature) in the left-sided distributions of cranial nerve V (V1,V2, and V3) and decreased power in the left orbicularis oculi.

Routine investigations were normal (Table 1). Magnetic resonance imaging (MRI) of the brain and spine were normal. Cerebrospinal fluid (CSF) analysis was notable for a white blood cell count of 28/mm^3 (85% lymphocytes, reactive) and protein concentration above the upper limit of normal (0.49 g/L). ZIKV RNA was detected from CSF via polymerase chain reaction (PCR). Serum PCR for ZIKV was negative but ZIKV IgM antibody was reactive, with plaque reduction neutralization test (PRNT) titers corroborating the molecular ZIKV diagnosis (Table 1).

The patient received supportive care in hospital over a 5-day admission. She did not receive intravenous immunoglobulin (IVIG). On discharge, she was able to ambulate with the assistance of a walker and continued to report headache, fatigue, weakness, and numbness in the left thigh. She was followed in the outpatient physiatry clinic for rehabilitation support and management of the post-infectious fatigue syndrome. She was prescribed gabapentin and celecoxib for the management of chronic neuropathic pain. After 1 month, she was able to return to work on a modified schedule required to accommodate the on-going muscle fatigue and weakness. At 4 months post-discharge, she was ambulating independently. Six months post-discharge, there was residual left hip flexor weakness (4/5), decreased light touch sensation in the left lower extremity, and on-going paresthesia with chronic neuropathic pain. Nerve conduction studies performed at that time were normal. By 2 years post-discharge, all symptoms and signs had resolved.

Methods

Mini-Review We performed a non-systematic mini-review of the English language literature using the PubMed database from inception to October 26, 2018, and combinations of the search terms "Zika*", "neurologic*", and "Guillain-Barre syndrome" in order to contextualize the demographic, clinical, and laboratory features of our patient with what is already known about the Guillain–Barre syndrome in ZIKV infection. Bibliographies of literature identified by our search strategy were also hand searched for additional relevant reports. We restricted our review to studies reporting primary data on clinical course, diagnosis, and treatment of Guillain–Barre syndrome in Zika and included all observational studies, case series, and case reports.

Discussion

Neurologic Sequelae of Zika Virus Infection

Most people infected with ZIKV suffer mild, if any, symptoms typically consisting of fever, rash, arthralgia, and non-purulent conjunctivitis [1]. The putative association with neurologic disorders was first made in the 2015 ZIKV outbreak in French Polynesia with a study which found that all of the

patients diagnosed with Guillain–Barré syndrome during the surveillance period had evidence of ZIKV infection [2•,3]. Since then, several case reports/series and surveillance reports from Latin American, South America, and Oceania have corroborated the association between ZIKV and Guillain–Barré syndrome [4, 5•, 6–8, 9••, 10–14, 15••, 16–23]. Zika virus infection has been associated with additional neurologic complications including sensory polyneuropathy, facial paralysis, vestibulitis, encephalitis/meningoencephalitis, myelitis, and a severe congenital ZIKV syndrome characterized by fetal/neonatal microcephaly and other central nervous system (CNS) abnormalities (reviewed in [24••, 25, 26].

The Guillain–Barré Syndrome

The Guillain–Barré syndrome is classically described as an immune-mediated, post-infectious acute polyradiculoneuropathy attributed to molecular mimicry between the antigenic epitopes of the inciting pathogen and 'self' neuronal proteins [27]. It is a known complication of many bacterial and viral infections including *Campylobacter jejunii*, *Mycoplasma pneumoniae*, *Haemophilus influenzae*, influenza virus, Epstein–Barr virus, cytomegalovirus, human immunodeficiency virus, and rarely the arboviruses dengue virus, chikungunya virus, and West Nile virus [27–29].

The Guillain–Barré syndrome features progressive, symmetric muscle weakness and diminished or absent deep tendon reflexes, but a spectrum of neurologic manifestations including facial muscle weakness and paresthesia of the hands and feet is well described. Symptoms typically evolve over 2 to 4 weeks following a period of latency after an acute infection or vaccination. Cerebrospinal fluid findings include elevated protein concentration with a white blood cell count < 50/mm^3 (the albuminocytologic dissociation), while nerve conduction studies (NCS) are useful in identifying specific disease variants.

Zika Virus-Associated Guillain–Barré Syndrome

The patient presented in the clinical vignette had many features consistent with the Guillain–Barré syndrome though the relatively short interval between the onset of ZIKV illness and neurologic symptoms, and the rapid progression to symptomatic nadir, are atypical of classic post-infectious Guillain–Barré syndrome. Emerging reports of Guillain–Barré-like syndromes from ZIKV-affected regions have described similar clinical profiles (Table 2). A case series conducted in Colombia found that almost half of the patients with proven ZIKV infection and Guillain–Barré syndrome manifested neurologic symptoms soon after onset of the viral illness; 40% had concurrent viremia at the time of their admission for management of the Guillain–Barré syndrome and 57% had positive ZIKV studies from CSF [5••]. These findings have led to speculation that neurologic sequelae of ZIKV infection may result from direct viral infection of peripheral nerves (reviewed in [30••]. Zika virus is phylogenetically related to other neurotropic flaviviruses such as West Nile virus and Japanese encephalitis virus, and the neurotropism of ZIKV has been well established in murine models [31]. However, while studies of human tissues are limited, a recent report of a sural nerve biopsy taken from a patient with ZIKV and Guillain–Barré syndrome did not detect ZIKV in nerve tissue [32, 33]. Alternatively, there is evidence of considerable peptide overlap between the ZIKV polyprotein and human neural proteins [34]. The ZIKV incubation period may provide the time required to generate cross-reactive antibodies, thus allowing concurrent manifestation of ZIKV and neurologic symptoms. Serum analyses have confirmed the presence of circulating autoantibodies in patients with ZIKV-associated Guillain–Barré syndrome, but the anti-ganglioside antibodies typically associated with the Guillain–Barré syndrome are rarely apparent [2•]. These observations raise the possibility that a novel host target is implicated ZIKV-induced Guillain–Barré syndrome [33].

The spectrum of clinical severity associated with Guillain–Barré-like syndrome following ZIKV infection is broad. Case series have reported rates of admission to intensive care units ranging from 38 to 69% and the need for assisted ventilation ranging from 29 to 35% [2•, 6, 7, 9••]. The majority of the patients reported in the literature received IVIG at the time of diagnosis; however, there have been no prospective or randomized clinical trials to evaluate the efficacy of this intervention or other modalities used in the management of classic Guillain–Barré syndrome, such as plasma exchange (PLEX), for the management of ZIKV-associated neurologic complications (Table 2). Nevertheless, the World Health Organization now recommends either IVIG or PLEX therapy for all patients with Guillain–Barré syndrome who have rapidly progressive symptoms, are unable to walk unaided, or who develop progressive bulbar weakness [35].

While patients reach the nadir of neurologic symptoms within a few days of onset, resolution requires a protracted period of recovery in keeping with the time required for repair of demyelinated peripheral nerves. Anaya and colleagues describe 29 patients with confirmed/probable ZIKV infection complicated by Guillain–Barré syndrome, over half of whom were bed- or chair-bound at the time of discharge [6]. Dirlikov and colleagues reported that 45% of patients in their cohort were discharged from hospital to a rehabilitation facility or a skilled nursing facility [23]. Among the cases reviewed in Table 2, most patients

Table 2 Similar clinical profiles

Study	Location/date	Interval from viral illness to GBS onset	GBS-associated symptoms	Management					Outcome	Diagnosis of ZIKV
		Median d [IQR]		ICU	ICU LOS	Asst Vent	IVIG	PLEX		
Ferreira *et a l*[4] *n = 4*	Pernambuco state, Brazil 12/2014–06/2015	4.5 range (3–5)	Not documented	–	–	–	**2** (100%)	–	(1) Residual LE weakness (2) Unable to ambulate (3) Complete Recovery after 45d (4) Persistent motor deficits, requires orthopedic supports	PCR: 100% (serum) Virus isolation: 40% (serum) ZIKV IgM: 40% (serum)
Cao-Lormeau et al [2] Watrin et al *3 n = 42*	French Polynesia 10/2013–03/2014	6 d [4–10]	Unable to walk unaided: 62%; Dysphagia: 45%; Motor weakness (limbs): 74%; Unilateral / Bilateral facial palsy: 19% / 60%; DTR absent/diminished: 88%; Neurogenic pain/paresthesia: 91%	16 (38%)	39 d [3–127]	12 (29%)	42 (100%)	1 (2%)	Death: 0 (0%) Ambulation at 3mo: 24 (57%)	PCR: 0% (CSF + serum) IgM/IgG: 98% (serum) Neutralizing Antibodies: 100%
Parra et al [5] *n = 35*	Colombia, 11/2015–03/2016	6 d [4,19]	Not available	–	–	–	–	–	Not documented	PCR: 17 (48.6%) (Urine 16, CSF 3, Serum 1) IgM/IgG: 32 (91.4%) (Serum 23, CSF, 25)
Anaya et al [6] *n = 42*	Colombia, 06/2015–07/2016	7 d [1–14.5]	Not available	29 (69%)	–	10 (34%)	22 (76%)	1 (3%)	Hughes' Functional Grade: **1:** 4/27 (14.8%); **2:** 5/27 (18.5%); **3:** 4/27 (14.8%); **4:** 14/27 (52%); **5, 6:** 0 (0%)	IgM/IgG: Positive (serum)
Villamil-Gomez et al [7] *n* = 16	Sucre, Colombia 2016	9 d [4.5–9]	Paresthesia: 85.%; Hypo/ areflexia: 69%; Symmetric weakness: 81%; Facial paralysis: 50%	16 (100%)	9 d [5.5–12]	2 (12.5%)	16 (100%)	0	Not documented	PCR: 100% *(source not documented)*
Simon et al [8] *n* = 5	New Caledonia 01/2014–02/2016	mean 9 d range (7–10)	Quadriparesis: 80% Deep tendon reflex alteration: 100% Sensory deficit: 80%, Facial diplegia: 100% Dysautotonia 40%; Impaired respiration: 0%	–	–	–	5 (100%)	–	*3 mo follow up:* Neuropathic pain (20%)	PCR: 0% IgM/IgG/PRN-T: 100% *(serum)*
da Silva et al [9] *n = 27*	Rio de Janeiro, Brazil 12/2015–05/2016	10 d range (4–22)	Back/LE pain: 63%; Symmetric UE + LE weakness: 19%; LE predominant: 82% Dysautotonia:	4 (15%)	0 d range (0–14)	2 (7%)	26 (96%)	0	Death: 1 (4%) *3 mo follow up:* Hughes Functional Grade: 1 (range 0–4) Chronic pain: 15 (56%)	Not documented

Table 2 (continued)

Study	Location/date	Interval from viral illness to GBS onset	GBS-associated symptoms	Management					Outcome	Diagnosis of ZIKV
			22%; Dysphagia: 11%; Facial weakness: 41%; bifacial weakness:19%; numbness: 11%; Other cranial neuropathies: 33%; Sensory deficit:74%; Ataxia: 70%; Absent/reduced reflexes: 89%							
Mehta et al [10] *n = 5*	Rio de Janeiro, Brazil 11/2015–06/2016	12 d range (5–41)	Flaccid areflexic quadriparesis 2 (40%) LL paraesthesia 100%; UL paraesthesia 60%; Facial nerve palsy 60%; Periorbital paresthesia 20%	2 (40%)	–	2 (40%)	5 (100%)	–	20% with no recovery at 3 weeks (ZIKV/CHKV co-infection) 20% with full recovery at 1 year 60% with improvement, not specified	PCR (CSF, serum, urine) or IgM (serum)
Rozé et al [11] *n = 2*	Martinique 01/2016	(1) 0 d (2) 0 d	(1) Numbness in all extremities, ataxia, constipation, flaccid tetraparesis, asymmetric facial palsy, deglutination disorder. (2) Numbness in all extremities, gait disturbance, constipation, flaccid tetraparesis, asymmetric facial palsy, respiratory failure	(1) Yes (2) Yes	(1) 10 d (2) 1 mo	(1) Yes (2) Yes	(1) Yes (2) Yes	(1) No (2) No		
Wright et al *current study n = 1*	Nicaragua 08/2016	1 d	Muscle weakness, unable to ambulate independently; reduced LE sensation; paresthesia in hands and feet, decreased vibration sense in feet, decreased reflexes, decreased sensation left CN V1–3 and decreased power to left facial nerve	No	N/A	No	No	No	Day5: discharge, unable to ambulate independently *1 mo follow up*: ambulating with assistance; modified return-to-work schedule; *4 mo follow up*:: ambulating independently *6 mo follow up*: left hip flexor weakness, decreased sensation LLE, chronic neuropathic pain *2 y follow up:* All symptoms resolved	PCR: Positive (CSF) IgM: Positive (serum)
Mancera-Paez et al [12] *n = 1*	Cúcuta, Colombia, 01/2014	1 d	Urinary retention, foot drop, bilateral LL weakness ascending to flaccid quadriplegia over two days;	Yes	6w	Yes	Yes	–	*At Discharge:* unilateral optic neuritis, generalized areflexia, flaccid paraplegia; sensory loss (C5-T2); loss of sensation, proprioception (T6	PCR: Positive (serum) IgG: Positive (PRNT>1/128)

Table 2 (continued)

Study	Location/date	Interval from viral illness to GBS onset	GBS-associated symptoms	Management					Outcome	Diagnosis of ZIKV
			confusion, hypoexemic respiratory failure. *Patient also developed transverse myelitis, ADEM, and encephalitis*						to LL); Discharged to Rehabilitation facility. *1 year follow up:* flaccid paraplagia with global arfelxia, wheel-chair bound, incontinent of bowels and bladder, absent sensation in LL bilaterally. Normal cognition.	
Thomas et al [13] *n = 1*	*Puerto Rico 01/2016*	3 d	Paresthesia hands and feet, bilateral muscle weakness (bulbar and limb), areflexia, dysautotonia	–	–	–	Yes	No	Not documented	PCR: Negative (serum, urine) IgM: Positive (serum)
Brasil et al [14] *n = 1*	Brazil 06/2014	5 d	Paresthesia hands/ft, LE weakness, decreased sensation, areflexia	–	–	–	–	–	Day 13: discharge, ambulating independently *Day 41 follow up*: fully functional, chronic headache	PCR: Positive (serum, CSF, saliva, urine)
Siu et al [15] *n = 1*	Tonga	6 d	Progressive/global weakness, numbness, decreased sensation hands and feet, impaired vibration sense in feet, ataxia, areflexia, respiratory failure	–	–	Yes	Yes	Yes	Respiratory status improved; extubated. Day 32: Discharge to Rehabilitation facility, bedbound with persistent global weakness (3/5)	PCR: Positive (serum), PCR: Negative (CSF) IgM: Positive (serum)
Oehler et al [16] *n = 1*	French Polynesia 11/2013	7 d	Paresthesia hands and feet, ascending muscle weakness, bilateral/asymmetric facial palsy, areflexia, dysautotonia	–	–	–	Yes	No	Discharge: paraparesis *Day40 follow up:* independent ambulation, muscle strength not fully recovered.	PCR: Negative (serum) IgM: Positive (serum)
Langerak et al [17] *n = 1*	Suriname 02/2016	7 d	Muscle weakness, paresthesia/pain in legs, areflexia.	–	–	No	No	No	Discharge: Unable to ambulate independently *4 month follow up*: remains dependent, unable to work. Can ambulate independently for a few steps	PCR: Positive (urine)
Miller et al [18] *n = 1*	Dominican Republic 05/2016	7 d	Rapidly progressive weakness, legs then arms. Day 7: flaccid tone, symmetric leg weakness proximal > distal; hyperaesthesia soles of feet; truncal ataxia, bi-brachial dysmetria; areflexia UE + LE, decreased	–	–	–	Yes	–	1 week post IVIg: improved weakness, paresthesia, ataxia, reflexes (upper limb) Day 20 post IVIg discharged to Rehabilitation Facility: ataxia - resolved; able to ambulate a few steps with assistance; reflexes normal	PCR: serum (negative) IgM: Positive (serum + CSF) PRNT: elevated titres ZIKV and DENV

Table 2 (continued)

Study	Location/date	Interval from viral illness to GBS onset	GBS-associated symptoms	Management					Outcome	Diagnosis of ZIKV
			vibration/proprioception to ankles/wrists							
do Rosário et al [19] n = 2	Brazil 05/2015	(1) 8 d (2) 10 d	(1) Tetraparesis, paresthesia hands and feet, bilateral asymmetric facial palsy, dysarthria, dysphagia, urinary and fecal incontinence, areflexia (2) Asymmetric tetraparesis, paresthesia hands/ft, bilateral facial nerve palsy, diplopia, dysphagia, areflexia, ataxia, fatigue	(1) Yes (2) No		(1) No (2) No	(1) Yes (2) Yes	(1) No (2) No	(1) Discharge: ambulating with assistance *Day 47 follow up*: normal strength, sensation; mild/mod residual right facial palsy and areflexia (2) *Day 58 follow up*: independent ambulation; normal strength, sensation and reflexes; mild residual bilateral facial palsy	(1) PCR: Negative (serum) IgM: Positive (serum) (2) PCR: Negative (serum) IgM: Positive (serum)
Hendel-Paterson et al [20] *n = 1*	Guyana 03/2016	9 d	Paresthesia hands and feet, ataxia, weakness requiring support to ambulate; reduced power, sensation in lower extremities; reduced reflexes	–	–	No	Yes	No	Discharge: minimal assistance in ambulation. *1 month follow up*: recovery of strength; ongoing paresthesia hand and feet; *2 month follow up*: on going paresthesia	PCR: Positive (serum, CSF, urine) IgM: Positive (serum, CSF)
Kassavetis et al [21] *n = 1*	Haiti 01/2016	several days	Facial diplegia, Ophthalmoplegia, Gait and upper extremity ataxia, areflexia	–	–	–	Yes	No	Discharge: ataxia requiring walking aid *Week 3 follow up*: resolved ophthalamoplegia, returned DTR; minimal improvement facial muscle weakness; required walking aid	IgM: Positive (serum, CSF)
Sebastian et al [22] *n = 1*	Multi-Site 12/2015–04/2016	–	Not documented	Yes	6d	–	Yes	–	Multi-system organ failure Discharge: minimal residual disability	PCR: 100% (serum or CSF)
Dirlikov et al [23] *n = 1*	Puerto Rico 02/2016	No viral pro-drome	Paresthesia and muscle weakness, UE + LE worsening over 8 days to respiratory distress requiring intubation	Yes	31d	Yes	Yes	No	Electrodiagnostic studies consistent with AIDP GBS variant. ICU course complicated by MDR ventilator-acquired pneumonia. Patient died 37 days after onset of neurologic symptoms.	PCR: Positive (urine) IgM: Positive (serum) *ZIKV RNA or antigen not identified in neural tissue on autopsy*

LOS length of stay, *ICU* intensive care unit admission, *AsstVent* assisted ventilation, *IVIg* intravenous immunoglobulin, *PLEX* plasma exchange, *CSF* cerebrospinal fluid, *d* days, *mo* months, *LE* lower extremities, *UE* upper extremities

Hughes' Functional Scale for disability post-discharge: 0 = healthy; 1 = minor symptoms or signs of neuropathy, but capable of manual work/running; 2 = able to walk without support × 5 m, but incapable of manual work/running; 3 = able to walk with assistance device; 4 = confined to bed or chair bound; 5 = requiring assisted ventilation; 6 = dead

with Guillain–Barré syndrome regained independent ambulation several weeks following infection. Neuropathic pain and paresthesia can take longer to resolve.

Conclusions

There has been an exponential rise in the number of reported ZIKV infections among travelers since 2013 [36••, 37–40]. A wide spectrum of acute ZIKV infection manifestations have been reported in Canadian travelers returning from South America and the Caribbean, including neurologic complications. Currently, the pathogenesis of ZIKV-associated Guillain–Barré syndrome is poorly understood. It may involve the classic mechanisms of immune-mediated polyradiculoneuropathy, or result from direct cytopathic effect of ZIKV infection, or both.

Returned travelers from ZIKV-endemic regions with onset of the Guillain–Barré-like syndrome warrant testing for markers of ZIKV infection, including PCR (serum, urine, CSF) and IgM/IgG serology (serum, CSF), and should be followed carefully until the nadir of the neurologic symptoms is established and the symptoms of active viremia have abated. Progressive neurologic compromise may necessitate monitoring and treatment in an intensive care unit. Zika virus-associated Guillain–Barré syndrome can result in long-term disability. Patients should be counseled to expect a protracted recovery period and may benefit from multidisciplinary rehabilitation therapy as well as pharmacologic therapy to manage neuropathic pain.

Authors' Contributions JKW contributed to literature review, data collection, analysis, and interpretation, and was primarily responsible for drafting the manuscript. LC contributed to literature review, data collection, analysis, and interpretation, and to critical appraisal of the manuscript. CL and AK contributed to literature review, data collection, and data analysis. MB contributed to data collection, data analysis, and to critical appraisal of the manuscript. AKB conceived the report and contributed to literature review, data analysis and interpretation, and to writing and revising the text.

Compliance with Ethical Standards

Conflict of Interest All authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Disclosures AKB serves on the Committee to Advise on Tropical Medicine and Travel (CATMAT), an external advisory body to the Public Health Agency of Canada.

Ethics Statement The patient described herein provided full informed consent for the report.

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- • Of importance
- •• Of major importance

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