

Rapid Communication

The re-emergence of Zika in Brazil in 2020: a case of Guillain Barré Syndrome during the low season for arboviral infections

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Report

Since emergence in Brazil in 2015, manifestations of Zika virus (ZIKV) infections range from asymptomatic to severe neurological complications, including Guillain Barré Syndrome (GBS) in adults and microcephaly in newborns via transplacental transmission.^{1,2} In 2015, a 4-fold increase in adult ZIKV infections was reported characterized by GBS cases with frequency similar to the 2013 French Polynesian ZIKV outbreak.³ Brazilian ZIKV infections fell from 2016 to 2019, suggesting that most susceptible individuals were infected during the initial epidemic, though animal reservoirs persist.⁴ Chikungunya virus (CHIKV) emerged in Brazil as another arbovirus associated with GBS.⁵ Here, we present a GBS case in northeastern Brazil outside the typical arboviral season.

As the rainy season ended, a 29-year-old man presented with 2 days of ascending paresthesia in feet, then paraparesis of lower extremities. Neurologic symptoms evolved to his trunk and upper extremities associated with respiratory distress, uri-

nary incontinence and dysphagia. Eight days prior, he noted myalgia and fever without rash, conjunctivitis, retro-orbital pain or diarrhea. He did not recall mosquito exposure; however, reported no regular use of repellent or screened windows. The rural area where he lived was affected during the ZIKV epidemic in 2015–16, with an incidence of over 300 cases per 100 000 inhabitants.

In the neurologic intensive care unit 48 hours after symptom onset, patient examination revealed dyspnea, proximal and distal sensory loss, tetraplegia and dysarthria with facial symmetry requiring mechanical ventilation. Laboratory results noted leukocytosis 13 600 mm³ (normal range: 3600–11 000 mm³) and erythrocyte sedimentation rate 59 mm/h (normal < 15 mm/h). Cerebrospinal fluid analyses were within normal range. At Day 33 from symptom onset, RT-qPCR of plasma, urine and oral swabs for ZIKV, DENV and CHIKV were negative (Supplemental Table 1). Serology for ZIKV (IgM, IgG, PRNT) was positive, negative for DENV (NS1, IgM, PRNT) and

negative for CHIKV by IgG and PRNT (though positive IgM) (Supplemental Tables 2 and 3).

No improvement in neurologic function occurred following intravenous immunoglobulin (IVIg, 40 g/day) initiated on Day 5 after symptom onset. Neurologic examination at discharge (Day 45) demonstrated 1 of 5 strength in lower extremities and 3 of 4 in upper extremities with bilateral areflexia and diminished general tactile sensation. Electromyography at Day 115 revealed motor and sensory polyradiculopathy, demyelination with re-innervation of right upper extremity muscles though ongoing active denervation bilaterally in lower extremities. By Day 195, he remained with diminished sensation and strength in the feet requiring a walker to ambulate. Despite early IVIg therapy, he remained severely impaired 6 months after disease onset. Long-term sequelae occur in up to 20% of ZIKV-GBS with ambulation disability lasting up to 1 year. Lack of an exhaustive search for alternative causes of GBS is a possible limitation, though his symptoms and laboratory findings were most consistent with arbovirus associated GBS.

Previous work during ZIKV and CHIKV-outbreaks in Brazil noted an association with GBS, a relationship other studies in Central and South America also found.⁵ This ZIKV- and CHIKV-associated GBS case highlights the ongoing importance of vigilance in residents and travelers to regions with prior ZIKV and CHIKV outbreaks, particularly outside typical arboviral seasons.

Supplementary data

Supplementary data are available at *JTM* online.

Authors' contribution

Conceived and designed the study: Ricardo Khouri, Viviane Boaventura, Kevan Michal Akrami and Betania Mara Freitas de Nogueira. Performed clinical evaluation: Kevan Michal Akrami, Betania Mara Freitas de Nogueira, Viviane Boaventura, Mateus Santana do Rosário, Isadora Cristina de Siqueira and Daniel Farias. Performed the experiments: Laíse de Moraes, Marli Tenório, Lillian Nunes Gomes, Isabele de Pádua Carvalho, Ellen

dos Reis Pimentel, Jéssica de Jesus Silva and Marcos Vinícius Lima de Oliveira Francisco. Analyzed the data: Ricardo Khouri, Viviane Boaventura and Kevan Michal Akrami. Wrote the paper: Ricardo Khouri, Viviane Boaventura and Kevan Michal Akrami. Supervised the project: Ricardo Khouri, Viviane Boaventura, Manoel Barral Netto and Aldina Barral. All authors provided critical feedback and helped shape the manuscript.

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Conflict of interest

All authors have disclosed no potential conflicts of interest.

References

1. Mlakar J, Korva M, Tul N *et al*. Zika virus associated with microcephaly. *N Engl J Med* 2016; **374**:951–8.
2. Styczynski AR, Malta JMAS, Krow-Lucal ER *et al*. Increased rates of Guillain-Barré syndrome associated with Zika virus outbreak in the Salvador metropolitan area, Brazil. *PLoS Negl Trop Dis* 2017; **11**:e0005869.
3. Araujo LM, Ferreira MLB, Nascimento OJ. Guillain-Barré syndrome associated with the Zika virus outbreak in Brazil. *Arq Neuropsiquiatr* 2016; **74**:253–5.
4. Berry N, Ferguson D, Ham C *et al*. High susceptibility, viral dynamics and persistence of South American Zika virus in new world monkey species. *Sci Rep* 2019; **9**:14495.
5. Mehta R, Soares CN, Medialdea-Carrera R *et al*. The spectrum of neurological disease associated with Zika and chikungunya viruses in adults in Rio de Janeiro, Brazil: a case series. *PLoS Negl Trop Dis* 2018; **12**:e0006212.