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Letter to the Editor

Reversible sensory polyneuropathy during an arboviral outbreak in Salvador, Bahia, Brazil

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Dear Editor,

Guillain-Barré syndrome (GBS), an acute, immune- mediated polyradiculoneuropathy, typically occurs in response to minor viral and bacterial infections. Associations between this syndrome and previous arboviral infection, such as dengue (DENV), chikungunya (CHIKV) or Zika virus (ZIKV), have been reported in some studies [1,2]. GBS usually manifests as generalized weakness and areflexia, accompanied by sensory and autonomic disturbances [3]. Mild neurologic syndromes associated with ZIKV infection have previously been described, characterized by short-term isolated sensory disturbances [4,5]. Here we describe five cases of reversible sensory polyneuropathy occurring during the 2015 arboviral outbreak in Salvador, Bahia-Brazil.

This article describes a case series of five patients admitted to two tertiary hospitals located in the city of Salvador during the 2015 outbreak of ZIKV, CHIKV and DENV in Brazil. This study was approved by the institutional review board of Fundação Oswaldo Cruz – Bahia (1184454/2015). All patients were provided a written term of consent prior to participation in this study.

Blood and cerebrospinal fluid (CSF) was collected upon admission and serological testing for arboviruses was performed to detect anti-DENV and anti-CHIKV IgG and IgM antibodies, as well as anti-ZIKV IgG antibodies, by enzyme immunoassay (ELISA) using the Euroimmun® commercial kit. Anti-Zika IgM antibodies were detected by an in-house capture ELISA (CDC-Atlanta) [6]. Serum samples were also tested in a plaque reduction neutralization test (PRNT) against ZIKV and CHIKV. Moreover, according to the recommendations of the Brazilian Ministry of Health and due to the time of sample collection (> 5 days between onset of symptoms and collection of the samples), the molecular diagnosis by PCR was not performed. [7]

Additional blood tests were conducted to rule out any alternative causes of muscular/peripheral nerve disorders. Electrophysiology studies (EMG and nerve conduction studies) were performed in two patients by a certified neurologist with specialized training in neuromuscular diseases. All examinations included nerve testing in both the upper and lower extremities and F-wave testing.

Five patients presented with predominant sensory symptoms: stocking-glove paresthesia (100%) and hypoesthesia (75%). No abnormalities in gait, cranial nerves or reflexes were noted. The Hughes functional scale (HFS) (grades: 0–6) was used to evaluate disease severity, with the highest values corresponding to the greatest degree of neurological dysfunction [8]. The neurological manifestations in these patients were considered mild (100% had HFS < 2) and only one required hospitalization. All of them reported previous acute viral symptoms. The mean duration of symptoms was 7.0 days ($\pm$ 3.08), and the mean difference between the onset of virus symptoms and neurological manifestation was 15.4 days ($\pm$ 10.31). EMG detected no abnormalities in the two patients tested. The mean CSF protein value was 26 mg/dL (RV $<$ 40 mg/dL). Muscle enzyme, inflammatory, serology testing (HIV, HTLV, CMV, EBV, HCV, HBV, syphilis) and other routine laboratory results were unremarkable.

Two patients tested positive for anti-CHIKV IgM antibodies. Another two patients exhibited positivity for anti-ZIKV antibodies (one IgG alone and the other IgM and IgG). Anti-DENV IgG antibodies were present in all patient's sera. No patients presented positivity for DENV IgM antibodies. PRNT assays indicated exposure to CHIKV in two subjects, whereas the serological findings for ZIKV exposure indicated a recent infection for two subjects, confirming the results obtained in ELISAs tests.

Several cases of GBS and other neurological syndrome related do ZIKV and CHIKV had already been reported [9,10]. However, isolated cases of a neurological syndrome characterized by a milder presentation than GBS, which did not meet GBS criteria due to a lack of clinical, ENM or CSF abnormalities, were previously described in association with ZIKV infection, termed as acute transient polyneuritis (ATP) or reversible sensory polyneuropathy (RSP) [4,5]. Here we report five patients with reversible sensory polyneuropathy, characterized as mild disease (HFS < 2), presenting with exclusive sensory disturbance and no alterations in CSF or EMG studies. Serology results demonstrated that all patients (100%) presented evidence of previous arboviral infection, while most patients (80%) demonstrated recent infection by ZIKV or CHIKV. Peripheral neuropathy related to CHIKV had already been described in previous reports [11], however, to best of our knowledge, this is the first report of two cases describing this specific subtype of peripheral neuropathy (RSP) with strong evidence of recent CHIKV infection. Association with ZIKV was previously reported in case series with similar clinical findings, hypothesizing that these may have been a direct neuropathic or inflammatory effect of ZIKV, characterized by reversible inflammation and sensory nerve swelling [4,5], and recently it was hypothesized that ZIKV could direct infect peripheral neurons and promote cell death [12]. This report should serve as an important reminder to physicians and health care professionals to be alert in identifying other forms of neurological diseases possibly related to ZIKV and CHIKV infection.

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