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Guillain-Barré syndrome in patients with a recent history of Zika in Cúcuta, Colombia: A descriptive case series of 19 patients from December 2015 to March 2016

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ABSTRACT

Purpose: Zika virus (ZIKV) infection is an emerging global threat and a public health problem in the Americas. Guillain-Barré syndrome (GBS) has been recently associated to ZIKV. This report presents a case series of GBS possibly associated to ZIKV.
Methods: Clinical and demographic data from patients with GBS treated in 5 intensive care units and with recent history of ZIKV in Cúcuta, Colombia were collected from December 1 2015 to April 30 2016. Electrophysiological examination, lumbar puncture, and reverse transcriptase–polymerase chain reaction for ZIKV were performed in 14, 10, and 1 patients, respectively.
Results: Nineteen patients with GBS and a recent history of acute viral syndrome compatible with ZIKV infection were studied (mean age, 44 years; range, 17-78). Neurologic symptoms developed at a median of 10 days after the onset of the viral symptoms. Albuminocytological dissociation was found in 8 cases. Electrophysiological criteria for acute motor axonal neuropathy were found in all patients tested. Five patients met level 1, 8 patients level 2, and 6 patients level 3 of diagnostic certainty for GBS in the Brighton classification. Fifteen patients required respiratory assistance, 16 received intravenous immunoglobulins, and 3 had plasmapheresis. Seventy-nine percent of patients were in Hughes GBS disability scale 4 to 5 at discharge and no patients died during the observation period. Acute ZIKV infection, confirmed by reverse transcriptase–polymerase chain reaction, was observed for 1 patient.
Conclusions: All cases of this GBS outbreak had a recent history ZIKV infection, reinforcing existing evidence for the association between GBS and ZIKV. Future genetic and immunologic studies are warranted to further investigate the cause of the outbreak in detail.

1. Introduction

Zika virus (ZIKV) infection is still a not well-known emerging disease. During the recent ZIKV outbreak that came to America in May 2015 [1], and to Colombia in September 2015 [2], Cúcuta was one of the Colombian cities with the highest incidence [3]. Cúcuta has a population of 850 000 inhabitants, it has intense trade activities on the border with Venezuela that facilitate the spread of communicable diseases and *Aedes aegypti* is endemic since 1883. From December 2015 to March 2016, we noticed an increase of acute immune-mediated neurologic disorders in the intensive care units (ICUs) of the 5 largest private clinics of the city, from about 10 cases per year to 20 patients in 3 months.

By May 26 2016, more than 40 countries in the Americas have confirmed the presence of autochthonous cases in the region [4]. In addition, a downward trend in the number of cases reported in the region, mainly in Colombia. But within this outbreak in our country there have been about 93 000 reported cases of infection compatible with ZIKV, with Norte de Santander being the number one department in Colombia with 9872 reported cases (10.6%) [3] and the second in incidence [5]. By 2014, French Polynesia had reported more than 10 000 people with ZIKV and 70 cases of neurologic complications and within them, the

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most frequent was the presentation of Guillain-Barré syndrome (GBS) [6,7]. According to the World Health Organization (WHO) reports, the GBS associated with ZIKV has been reported in 13 countries, including Colombia and Venezuela [8]. In addition, there have been reports of other neurologic syndromes associated with ZIKV, such as acute myelitis and meningoencephalitis [9,10]. To our knowledge, there are no published reports of the clinical characteristics of patients with GBS groups in Latin America related to the outbreak of ZIKV.

We present this publication with 2 objectives: first, show which was the clinical behavior of patients and the response by the health system in an event not expected in the outbreak ZIKV and secondly, analyzing the electrophysiological classification and severity of GBS.

2. Methods

From December 2015 to March 2016, 20 patients were admitted to ICUs from Cúcuta, Colombia and were initially diagnosed with GBS. One patient was finally diagnosed with acute transverse myelitis, but full clinical description is not reported here. Demographic and clinical data of the 19 patients with GBS were obtained from medical records and are presented descriptively. The diagnosis of GBS was made based on a history of progressive weakness of the limbs within a period of 4 weeks associated with absent or diminished deep tendon reflexes. Diagnostic tests were not available for all patients. Clinical findings after treatment were evaluated according to the Hughes GBS disability scale [11].

Serological samples were collected and sent to the national reference laboratory of the Instituto Nacional de Salud (INS) for reverse transcriptase–polymerase chain reaction (RT-PCR) of ZIKV, because specific laboratory tests were not available in the city. At the INS, diagnosis of ZIKV was done with a validated RT-PCR protocol [5].

The interim clinical case definition developed by the WHO for suspected cases of ZIKV disease in geographic areas with autochthonous transmission [12] was used, which is similar to the definition of the INS of "confirmed cases by clinical criteria". Written informed consent was obtained from every patient and the institutional ethics research review board approved the study.

3. Results

A total of 19 patients finally diagnosed with GBS were admitted in 5 ICUs during the 3-month study period. An overview of the patient characteristics is shown in Table 1. The mean age of the patients with GBS was 44 years (range, 17-78) of which 12 (63.2%) were male. In addition, one patient was diagnosed with acute transverse myelitis. The first case of GBS presented on week 10 of the Cúcuta ZIKV outbreak (Fig. 1). All patients were of low socioeconomic status, with a median of 11 years of education, and at least 4 patients (21%) had occupational exposure to organic solvents such as fuels.

All patients had lower limb weakness and diminished or absent deep tendon reflexes. Lower limb areflexia was a characteristic feature in 18 (95%) cases whereas upper limb areflexia was observed in 8 (42%) patients. Other features like paresthesia, facial palsy, and acute oropharyngeal palsy were present in 14 (73%), 8 (42%), and 5 cases (26%), respectively. We also observed labile blood pressure in 15 (79%) cases, arrhythmias in 13 (68%) cases, adynamic ileus in 4 (21%) cases, and urinary retention was noted in 1 (5%) patient.

In this case series, all patients had a recent history of acute viral syndrome compatible with ZIKV infection in preceding 8 weeks with a median of 10 days (interquartile range [IQR], 5-12; range, 2-60) before the onset of neurologic manifestations. Of these antecedent symptoms, rash was found in 17 (89%) cases, fever in 15 (79%) cases, arthralgia in 14 (74%) cases, conjunctivitis in 7 (37%), and diarrhea in 4 (21%) patients. Six patients (32%) had underlying conditions. Four patients had hypertension, 1 patient had hypertension and diabetes mellitus, and 1 had a chronic kidney disease.

Lumbar puncture was performed in 10 (53%) patients. Cerebrospinal fluid evaluation showed albuminocytological dissociation in 8 cases and cerebrospinal fluid pleocytosis in 2 cases. Only 14 (73%) patients underwent electrophysiological examination performed within a mean of 35 days (range, 4-78 days). Ten cases (53%) showed findings suggestive of an acute motor axonal neuropathy (AMAN), such as prolongation of distal motor latencies, and decreased amplitudes of compound motor potentials without greater affectation of motor conduction velocities. The conduction velocities of mixed nerves such as the median and ulnar also had impaired sensory latencies, and also the sural nerve was found normal, findings consistent with AMAN subtype neuropathy. In addition, 2 cases (11%) showed unexcitable nerves, and we did not find any abnormality in another 2 patients (tested at days 7 and 11).

Of the 19 patients, RT-PCR was performed only in one patient with a positive result. The mean duration from onset of neurologic symptoms to initial treatment was 8 days (IQR, 5-11). Over the course of the disease, 15 (79%) patients required respiratory assistance. In addition to supportive care and respiratory management, 16 (84%) cases received

Table 1
Demographic and clinical characteristics of the GBS patients

Patient	Age/Sex	Limb paresis	Lower limb areflexia	Facial palsy	Paresthesias	Labile blood pressure	ACD	Brighton criteria
1	51/M	U, L	Yes	No	No	Yes	Yes	1*
2	78/M	L	Yes	No	Yes	Yes	Yes	1
3	69/F	U, L	Yes	Yes	Yes	No	Yes	1
4	35/M	L	No	No	No	Yes	Yes	1
5	17/M	U, L	Yes	Yes	Yes	Yes	Yes	1
6	69/M	U, L	Yes	No	Yes	Yes	NP	2
7	58/F	U, L	Yes	No	Yes	Yes	NP	2
8	61/F	U, L	Yes	No	No	Yes	Yes	2
9	60/F	L	Yes	Yes	Yes	Yes	NP	2
10	45/M	L	Yes	Yes	Yes	Yes	NP	2
11	34/M	U, L	Yes	No	Yes	Yes	NP	2
12	18/M	U, L	Yes	No	Yes	No	Yes	2
13	56/M	L	Yes	Yes	No	Yes	Yes	2
14	42/F	U, L	Yes	No	Yes	Yes	NP	3
15	44/F	U, L	Yes	Yes	Yes	Yes	NP	3
16	22/M	U, L	Yes	Yes	Yes	No	NP	3
17	27/M	U, L	Yes	No	No	Yes	No	3
18	27/F	U, L	Yes	No	Yes	Yes	No	3
19	26/M	L	Yes	Yes	Yes	No	NP	3
Total Number (%)	M: 12 (63.2)	U: 13 (68.4) L: 19 (100)	18 (95)	8 (42.1)	14 (73.7)	15 (79)	8 (42.1)	

M indicates male; F, female; U, upper; L, lower; ACD, albuminocytological dissociation; NP, not performed.
* RT-PCR positive.