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**Guillain-Barré syndrome** **associated with Zika virus infection**

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**CASE REPORT**

A 24-year-old housekeeper was admitted to hospital in Rio de Janeiro, June 2014, with headache, fever and rash. Five days earlier she had woken with a severe generalized headache and retro-orbital pain; she was very weak with paresthesia of the extremities. After two days she became febrile, (axillary temperature 42ºC), with chills, and a pruritic rash on the face, abdomen, chest and arms (Figure 1a). By day four, she was afebrile but had severe painful swelling of the hands (Figure 1b) and feet, weakness, difficulty walking, and a disseminated pruritic rash. She was admitted the next day. She had dengue five years previously. She had not traveled recently, and did not recall tick or mosquito bites.

On examination, the patient was alert and fully oriented, with axillary temperature of 36.7°C, pulse 90/minute, blood pressure 100/60mmHg, and respiratory rate of 20/minute. She had a diffuse erythematous macular rash, bilateral non-purulent conjunctival hyperemia, enanthema of the palate, an enlarged painless cervical lymph node, and severe hand and feet swelling, but no meningeal signs. Strength was reduced in the lower limbs and she could not walk. She had absent deep tendon reflexes at the knees and ankles, and both plantars were absent; there was reduced sensation to light touch distally in the legs, but no urinary retention or ataxia. The remainder of the examination, including neurological examination of the arms was normal. A lumbar puncture was normal (day 6), as were nerve conduction studies and an electromyogram (day 10), and a non-enhanced magnetic resonance imaging scan (day 13). From day 10 the rash and swelling began to resolve. By day 13 she was fully mobile and discharged. At follow up (day 41) her only remaining symptoms was persistent headache.

Because of the clinical presentation the patient’s serum and cerebrospinal fluid (CSF) were investigated for dengue, chikungunya and Zika viruses. Real-time PCR for dengue and chikungunya was negative, but PCR was positive for Zika virus1 in serum (day 5), CSF (day 6), saliva (day 10) and urine (day 11). CSF, acute and convalescent serum were negative for dengue and chikungunya by IgM-capture ELISA. No Zika ELISA was available. In order to identify the Zika virus genotype, 327 base pair amplicons encompassing the envelope protein were sequenced**,** and the Asian lineage of Zika identified in the CSF (Fig 2).

The mosquito-borne Zika vírus (family *Flaviviridae*, genus *Flavivirus)* was first isolated from a rhesus monkey in the Zika Forest, Uganda in 1947 and identified in humans in 1952. Since then there have been occasional cases in Africa and Asia, a small outbreak in Yap Micronesia in 2007, and a larger outbreak in French Polynesia in 2013, with 31,000 suspected cases2

Like dengue and chikungunya viruses, Zika virus causes a febrile illness with rash; its Importance in neurological disease remains to be seen. During the Polynesia outbreak in 2013, an apparent increase in Guillain-Barré syndrome (GBS) incidence was noted although there were no baseline data for comparison; 3 a single case was described in more detail.4 This was a patient with antibodies against Zika and dengue viruses, which can also trigger GBS,5 but no virus detected; so Zika’s role was uncertain.

In our patient there was no evidence of dengue or chikungunya infection, but Zika was found by PCR in the CSF. Our patient also, unusually, had high grade fever and clinical features consistent with paraparetic GBS, a rare atypical presentation.6,7,8 The CSF and neurophysiological investigations were normal, as is often found early in GBS. According to the “Brighton” GBS classification, she would meet Level III of diagnostic certainty (consistent clinical features, but without supporting CSF and neurophysiology evidence).6

Our case confirms the ability of Zika virus to enter the central nervous system, and highlights the need to think of this emerging virus as a mosquito-borne cause of fever, rash and neurological disease. Further work is needed to delineate the full spectrum of neurological manifestations of Zika infection.

**Consent**

This work was approved by the IPEC-FIOCRUZ Ethics Committee No. 0026.0.009.000-07 and the patient agreed to participate. Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review.

**Competing interests**

The authors declare that they have no competing interests.

**Authors´ contributions**

Patricia Brasil, conceived and coordinated the study, followed the patient, and drafted the initial manuscript. Andre Siqueira, Rogerio Valls, Guilherme Calvet, Andrea D´Ávila, Heruza Zogbi followed the patient and contributed to the manuscript. Tom Salomon drafted and revised the manuscript. Patricia Sequeira, Ana Bispo, Rita Nogueira, Marcos Mendonça carried out the molecular genetic studies, participated in the sequence alignment and helped draft the manuscript. All authors contributed to the management through discussing the case and implications of the results. All authors read and approved the final manuscript.

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**Figure Legend**

Figure 1: Photos depicting the physical examination of the patient: **A** pruritic rash in the left upper limb; **B** severe swelling of the hands at admission; **C** hands after recovery.

Figure 2: Maximum likelihood phylogenetic tree from partial Protein E coding region of Zika virus. The Phylogenetic tree was constructed in MEGA 6.06 software, by 1000 bootstrap replicates, (support values greater than 75% shown) by using Tamura-Nei 93 model with invariant sites correction (Chosen by AIC Criteria). The branch length is indicated below of branch. Square represents ZIKV detected in CSF specimen.