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## CASE REPORT

# ACUTE INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (GUILLAIN-BARRÉ SYNDROME) FOLLOWING DENGUE FEVER

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### SUMMARY

This paper reports a case of dengue in a six-year-old female child who suddenly developed excruciating headaches, fever, myalgia and paresis. Laboratory examinations included blood count, platelet count, biochemical tests (BUN, creatinine, aminotransferases, and total bilirubin and bilirubin fractions) and specific IgM titers (enzyme-immunoassay with recombinant tetravalent dengue). After ten days of hospitalization and having already been in a home environment, a new clinical image emerged, characterized by dysphagia, dysphonia, weakness, peripheral facial palsy and paresthesia. The diagnosis of Guillain-Barré Syndrome was based on clinical findings, cerebrospinal fluid examination, electrophysiological findings and the exclusion of other pathologies. Our case, as some shown in previous reports, calls attention to the possibility that Guillain-Barré Syndrome may occur in association with dengue.

**KEYWORDS:** Acute inflammatory demyelinating polyradiculoneuropathy; Dengue fever; Guillain-Barré Syndrome; Neurological dengue.

### INTRODUCTION

Dengue is an acute febrile infectious disease caused by arboviruses, which belongs to the *Flaviviridae* family and are transmitted by two species of mosquitoes, the *Aedes aegypti* (which is the most common) and the *A. albopictus*[4,7]. To date, four serotypes are known: (DEN-1, DEN-2, DEN-3 and DEN-4)[7]. According to estimates by the World Health Organization, about 80 million people become infected annually and between 2.5 and three billion people are at risk of infection in 100 countries in all continents, except Europe[4,7].

Guillain-Barré Syndrome (GBS) is an acute inflammatory demyelinating polyneuroradiculopathy that often develops after infection, mainly viral infection. Cytomegalovirus, Epstein-Barr Virus and HIV are some of the viral agents associated with this neurological syndrome. Some studies call attention to the possible association between dengue and GBS[8].

We report a case of a six-year-old female who developed GBS 20 days after the onset of dengue symptoms. This report was approved by the Institutional Ethics Committee and the patient's legal guardian signed a free and clear consent form written in terminology that is easy to understand.

### CASE REPORT

ARN, female, six-year-old child was seen on January 2, 2011 at University Hospital with an excruciating headache, osteomioarticular pain, muscle weakness and fever. She was diagnosed with dengue fever 24 hours later and was hospitalized for ten days. The diagnosis was confirmed after clinical research examinations, which included blood count, platelet count, biochemical tests (BUN, creatinine, aminotransferases, and total bilirubin and bilirubin fractions) and by specific IgM titers (enzyme-immunoassay with recombinant tetravalent dengue) (Table 1).

On January 22, 2011, ten days after discharge, the patient began presenting dysphagia, dysphonia, vomiting and ascending paresthesia (predominantly in the distal third of the limbs). She was referred to the Pediatric Intensive Care Unit (PICU) with what appeared to be tetraparesis, peripheral facial paralysis of the right side, paralysis of eye movements and anarthria. Six days later the patient was diagnosed with GBS, based on cerebrospinal fluid examination (analysis showed lymphocytic pleocytosis with a normal glucose value and negative bacterial and fungal cultures) (Table 2), electrophysiological findings and the exclusion of other pathologies. Electrophysiology in this patient disclosed an abnormal demyelination pattern. She remained hospitalized for 20 days with medication (intravenous immunoglobulin

**Conflict of Interest:** None

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**Table 1**
Lab tests in a case of Guillain-Barré syndrome following dengue fever in a six-year-old child

| Lab test | Jan, 2 | Jan, 22 | Feb, 10 |
|---|---|---|---|
| Hemogram | | | |
| Erythrocytes (x$10^6$/$mm^3$) | 4.3 | 4.1 | 4.3 |
| Hemoglobin (g/dL) | 12.5 | 12.0 | 12.5 |
| Hematocrit (%) | 38 | 36.0 | 38.0 |
| RDW (%) | 12.5 | 13.0 | 13.5 |
| Leukocytes (/$mm^3$) | 3100 | 3000 | 7000 |
| Platelets (/$mm^3$) | 130000 | 90000 | 140000 |
| Urea (mg/dL) | 35 | 35 | 40 |
| Creatinine (mg/dL) | 1.1 | 1.2 | 0.9 |
| Total Bilirubin (mg/dL) | 1.6 | 1.9 | 1.1 |
| AST (U/L) | 70 | 65 | 35 |
| ALT (U/L) | 80 | 80 | 40 |
| Serology for dengue | | IgM 2.7 | IgM 3.3 |
| | | IgG < 0.9 | IgG 5.4 |

RDW - Red Cell Distribution Width; AST - Aspartato Aminotransferase; ALT - Alanina Aminotransferase.

**Table 2**
Cerebrospinal fluid (CSF) in a case of Guillain-Barré Syndrome following dengue fever in a six-year-old child

| Lab test | January, 22 | February, 10 |
|---|---|---|
| Glucose (mg/dL) | 45 | 40 |
| Protein (mg/dL) | 120 | 360 |
| WBCs (cells/μL) | 80 | 60 |
| Cell differential | 75% lymphocytes | 85% lymphocytes |
| Culture | Negative | Negative |

WBC - White Blood Cells.

400 mg/kg/day per five days) and ventilatory support as well as rehabilitation. She returned to daily activities and recovered her gait patterns after two months of rehabilitation.

At the neurological examination held on May 10, 2011, residual sequelae were found. The physical examination showed tetraparesis and sensory disorders (tactile hypoesthesia, temperature and pain in the distal third of the limbs, and hypopallesthestia). The patient recovered completely from the neurologic impairment caused by the involvement of the nuclei of the cranial nerves, except for the pitch and intensity of her voice (dysphonia). The gait patterns were unchanged; however, the speed as well as the timing of the ascent and descent of stairs was affected. With exception to the patellar reflex (bilateral hyporeflexia), the remaining deep reflexes also appear unaffected. Because the patient reports instability and insecurity while walking, she was directed to continue with rehabilitation.

## DISCUSSION

Dengue is the most common human arboviral infection and has been recognized as a clinical entity since 1780[6]. During the nineteenth century, dengue was considered a sporadic disease, causing epidemics at long intervals. However, dramatic changes in this pattern occurred and currently dengue is considered the most common viral disease transmitted by mosquitoes across the globe, being endemic in 112 countries. In tropical countries, annual outbreaks have occurred since 1986[3].

In most cases, the disease has a self-limited course, with nonspecific symptoms such as fever, feeling ill and weakness. The most striking characteristics include intense muscle pain and retro-ocular headache, which may or may not be associated with a cutaneous rash[8].

Many neurological symptoms are associated with dengue and have been recognized for over a century. The classic signs of acute infection are headache, dizziness, lightheadedness, insomnia, agitation, irritability and depression. A minority of symptoms manifests as encephalopathy. The post-infectious sequelae are mainly amnesia, dementia, manic psychosis, Reye's syndrome and meningoencephalitis[3]. However, most cases do not describe demyelination as a specific complication. Laboratory tests show elevated liver enzymes, leukopenia and thrombocytopenia, but these changes are not specific to dengue[1].

Despite frequent and severe dengue epidemics, there have been few reported cases involving neurological complications associated with the infection of this virus. This fact can be explained because, unlike other arboviruses[2], this virus rarely affects the central nervous system. The pathophysiology of these neurological complications can be explained by the occurrence of cerebral edema, cerebral hemorrhage, hyponatremia, liver failure associated with portasystemic encephalopathy, cerebral anoxia, microcapillary hemorrhage and/or the release of toxic products, which can occur separately or together[9]. Among the neurological manifestations that appear post-dengue, which may occur after the dengue fever and the following hemorrhagic dengue, post-infectious encephalitis, meningoencephalomyelitis, transverse myelitis, epilepsy, tremors, Bell's palsy, mononeuropathies and GBS stand out[5].

GBS occurs at an incidence of between 0.6 and 1.9 per 100,000 inhabitants and is characterized by ascending flaccid paralysis, deep areflexia and sensory changes. The examination of the cerebrospinal fluid reveals an albumin-cytologic dissociation.

Some previous reports, as with our case, call attention to the possibility that GBS may occur in association with dengue[3], although the mechanisms that relate to this infection are not known. However, there is evidence that this is an immune-mediated neurological disease[9]. The same pro-inflammatory substances that participate in the immune response to the dengue virus (tumor necrosis factor-α, complement, interleukins) also have an important role in the pathogenesis of GBS, which can establish the relationship between the two conditions[5]. In all previous reports, the onset of GBS occurred after the recovery of the initial infection. This fact was also observed in the patient in question.

The first report of post-dengue infection GBS in children is referred in the study of SULEKHA *et al.*[10]. The authors describe three children, all under the age of eight, who suddenly experienced ascending motor paralysis, sensory disturbances and albumin-cytological dissociation in the CSF after being infected by dengue some days before.

In 2004 CUNHA-MATTA *et al.*[1] reported the case of a 14-year-old

patient with what appeared to be ascending flaccid, areflexic tetraparesis, with electrophysiological findings consistent with GBS, beginning ten days after the classical form of dengue appeared. There was a complete functional recuperation, leaving only a deep areflexia. This recovery also occurred in our patient who, after recovery, was able to walk without support for independent daily living activities, although there were some residual sequelae.

## CONCLUSION

Our case calls for special attention because the dengue infection remains a serious public health problem in many countries and yet little is known about the actual incidence of neurological complications caused by the infection of the dengue virus. Therefore, it is important to consider dengue as a possible cause of GBS.

## RESUMO

**Polirradiculoneuropatia desmielinizante inflamatória aguda (síndrome de Guillain-Barré) após dengue**

Este trabalho relata o caso de uma criança, sexo feminino, seis anos que desenvolveu subitamente cefaléia lancinante, febre, mialgia e paresia. Os exames de investigação clínica, que incluíram hemograma, contagem de plaquetas, dosagens bioquímicas (uréia, creatinina, transferases e billirrubina total e frações) e por títulos específicos de IgM, por enzima-imunoensaio (EIA) com antígeno tetravalente de dengue. Após dez dias de internação e já em ambiente domiciliar, novo quadro clínico surgiu caracterizado por disfagia, disfonia, paresia, paralisia facial periférica e parestesias. O diagnóstico do dengue e da Síndrome de Guillain-Barré foi baseado nos achados clínicos, no exame do líquido cefalorraquidiano, achados eletrofisiológicos e na exclusão de outras patologias. Neste caso, como em alguns relato anteriores, chama a atenção para a possibilidade de que Síndrome de Guillain-Barré pode ocorrer em associação com a dengue.

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