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Case Report

Guillain–Barré syndrome complicating dengue fever: Two case reports

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ABSTRACT

Guillain–Barré syndrome is a rare neurological manifestation associated with dengue infection. More common antecedent infections include *Campylobacter jejuni* and Cytomegalovirus infection. Here, we report two cases of Guillain–Barré syndrome complicating dengue infection.

1. Introduction

Dengue fever is a mosquito-borne infection caused by an arbovirus and transmitted by Aedes mosquitoes. It is endemic in Malaysia with an increasing number of cases reported every year [1]. In 2009, the World Health Organization included neurological manifestations as one of the diagnostic criteria for severe dengue, recognizing the importance of neurological involvement in dengue infection [2]. These neurological manifestations can be subcategorized into encephalopathy, encephalitis, immune-mediated syndromes, dengue muscle dysfunction, and neuro-ophthalmic disorders [3].

Guillain–Barré syndrome (GBS) is an immune-mediated disorder characterized by acute areflexic paralysis with albuminocytologic dissociation. Variants of GBS include acute inflammatory demyelinating polyneuropathy, acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy, and Miller Fisher syndrome [4]. Patients with GBS can present with a wide spectrum of clinical manifestations ranging from mild self-limiting disease to acute fulminant cases with respiratory paralysis [5]. Compared with other infections such as *Campylobacter jejuni* and cytomegalovirus, dengue fever is an uncommon antecedent of GBS and only a few cases have been reported [6–9]. Here, we report two cases of dengue fever complicated by GBS.

2. Case Reports

2.1. Case 1

A 35 year-old man presented with a history of fever, chills, and rigors associated with nausea and vomiting for 4 days. He had no abdominal pain or bleeding tendency. In addition, he complained of bilateral lower limb weakness and had been unable to ambulate since the onset of fever.

Upon arrival, his clinical parameters were stable. He was well perfused with a capillary refilling time of < 2 seconds and a good pulse volume. Neurological examination revealed reduced distal muscle power (3/5) on dorsi- and plantar flexion bilaterally. The lower limb reflexes were diminished with a downgoing Babinski response. Sensation was diminished in both lower limbs, predominantly along the L4 and L5 dermatomes. There was no involvement of sphincter reflexes or the upper limbs. Examination of the abdomen and respiratory and cardiovascular systems revealed no abnormalities.

Conflict of interests: none.

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The initial laboratory investigation showed a normal hemoglobin level with a hematocrit of 42.9%, thrombocytopenia (134×10^9/L), and a normal white cell count. (4.27×10^9/L). His renal function, liver function, serum electrolytes, and creatine kinase were within the normal ranges. Dengue nonstructural protein-1 antigen was positive. A lumbar puncture was deferred as the patient did not consent to the procedure. A subsequent nerve conduction study (NCS) was consistent with axonal motor polyneuropathy affecting both lower limbs.

A diagnosis of GBS complicating dengue fever was made and he was treated accordingly. He was monitored closely for ascending weakness and respiratory muscle involvement. As his neurological deficit was mild, he did not receive any form of immunotherapy. He recovered from the acute illness and was discharged with residual weakness in ankle joint movement bilaterally. He was referred for further physiotherapy and occupational therapy. At the 3-month follow-up, there was marked improvement of muscle power and he was able to walk without aids.

2.2. Case 2

A 52 year-old man presented with progressive, ascending weakness of both lower limbs for 3 days. He had no facial asymmetry, slurred speech, or dysphagia. No sphincter involvement was noted. He had been discharged from the hospital 1 week previously for dengue fever which was nonstructural protein-1 antigen positive. Upon examination, his vital signs were stable. His peak expiratory flow rate was 360 mL/min. Neurological examination revealed severe weakness of the lower limbs, and he was unable to move either of his lower limb muscle groups against gravity. Patellar reflexes were absent but sensation was intact. His upper limbs were weak over the distal muscles with areflexia. Examination of the cranial nerves was normal. Examination of the cardiovascular and respiratory systems showed no abnormalities. Initial laboratory investigation revealed a hematocrit of 50%, and normal leucocyte and platelet counts. The renal profile was normal but liver function tests showed mild transaminitis (alanine transaminase 111 IU/mL).

A lumbar puncture was performed and cerebrospinal fluid (CSF) examination revealed albuminocytologic dissociation consistent with a diagnosis of GBS (Table 1).

He was started on a 5-day course of intravenous immunoglobulin (IVIG) 400 mg/kg/d. He was closely monitored for progression of disease, especially respiratory muscle involvement. On his 4th hospital day, his condition deteriorated and he developed respiratory muscle paralysis requiring mechanical ventilation. Unfortunately, his condition was further complicated by episodes of health care-associated infection and multiorgan failure. He died after 3 weeks in the intensive care unit.

Table 1
Clinical features and investigations for patient 1 and patient 2.

Features	Patient 1	Patient 2
Duration of preceding dengue infection (d)	4	7
Clinical presentations	Bilateral lower limbs weakness	Progressive ascending weakness on both lower limbs with respiratory muscle involvement
Neurological examination	Distal weakness with areflexia	Bilateral upper & lower limbs weakness with areflexia
Lumbar puncture & CSF findings	Not performed	Albuminocytologic dissociation
Nerve conduction studies	Axonal motor polyneuropathy	Not performed
Clinical outcome	Good recovery	Dead (due to ventilator-associated pneumonia)

CSF = cerebrospinal fluid.

3. Discussion

Dengue fever is a common mosquito-borne infection in tropical and subtropical countries and has a wide spectrum of clinical manifestations. The association between dengue fever and neurological manifestations is relatively uncommon. Only 1–5% of dengue cases were reported to have neurological involvement [10]. The two most common neurological complications of dengue are encephalopathy and encephalitis. Other manifestations include myelitis, myositis, GBS, and polyneuropathy [11]. Dengue has four distinct but closely related serotypes (DEN-1, DEN-2, DEN-3, and DEN-4). Of these, DEN-2 and DEN-3 are the most frequently reported serotypes in association with severe neurological disease [11].

GBS has an incidence of 0.6–1.9 per 100,000 population. It is characterized by ascending paralysis, areflexia, and sensory changes [6]. It is the most common peripheral nervous system complication of dengue fever, and is usually reported during the recovery phase of the illness [12]. AMAN is a rare variant of GBS classified based on NCS [4]. There are numerous case reports and case series on dengue with GBS. A wide spectrum of clinical manifestations are documented, ranging from mild motor weakness to debilitating quadriparesis and respiratory weakness requiring mechanical ventilation [9,13]. Therefore, high clinical suspicion is important to identify patients with GBS complications.

Our first patient developed symmetrical bilateral lower limb weakness at the onset of dengue fever. This is relatively uncommon as in most reported cases the onset of weakness was 1 week after dengue infection [3]. There was no ascending weakness and he improved clinically prior to discharge. The second patient had a more severe disease progression with debilitating quadriparesis and subsequent respiratory muscle paralysis requiring prolonged mechanical ventilation complicated by sepsis. The onset of muscle weakness was 5 days after the acute illness. These two cases demonstrate the two different ends of the clinical spectrum of GBS complicating dengue infection (Table 2). The close relationship between dengue and the onset of GBS strongly suggests that dengue is a preceding infection. In patients with such presentations, other diagnoses need to be excluded, such as hypokalemic paralysis and acute myopathy. These two diagnoses were unlikely as the patients had normal serum electrolyte and creatine kinase levels.

The essential investigations in GBS include lumbar puncture and NCS. CSF analysis might show increased protein concentration without pleocytosis (albuminocytologic dissociation), while NCS will show features consistent with demyelinating polyneuropathy [4]. Although a lumbar puncture was not performed in our first patient, NCS supported the diagnosis of AMAN with reduced conduction affecting both lower limbs. CSF analysis in our second patient was consistent with the diagnosis of GBS.

The mainstay of treatment in GBS is plasmapheresis and IVIG. Corticosteroids have been proven ineffective as reported in several studies [14]. When treatment is initiated within 2 weeks of disease

Table 2
Cerebrospinal fluid examination of patient 2.

Parameters	Results
Glucose	4.86 mmol/L
Protein	778 mg/dL
White cell count	0 cells/μL
Culture	Negative

onset, IVIG is reported to be as effective as plasma exchange in patients with GBS who cannot walk independently [15]. Complications such as autonomic dysfunction, sepsis, and deep vein thrombosis need to be treated aggressively during the progress of the disease [4]. The first patient presented with mild disease, and thus, no treatment was initiated. There was no progression of disease after admission and he recovered with minimal deficits following rehabilitation. By contrast, the second patient was started on immunotherapy upon diagnosis due to the severity of the illness. However, he later developed respiratory muscle paralysis and required mechanical ventilation. Unfortunately, he died.

The prognosis of GBS is generally favorable, but it is associated with mortality in approximately 10% in patients with severe disease, especially when there are complications from prolonged ventilation [14]. Recognizing complications, especially respiratory failure, is important for early intervention to reduce morbidity and mortality in severe disease. Despite immunotherapy and optimal support, around 20% of patients develop long term disability [16].

4. Conclusions

Dengue fever remains a serious global public health problem. Although it is rare, GBS should be as a differential diagnosis when patients present with weakness after dengue infection. With the surge of dengue cases, awareness of this condition is extremely crucial to reduce the morbidity and mortality.

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