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Sensory Predominant Guillain-Barré Syndrome Concomitant with Dengue Infection: A Case Report

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Abstract
Guillain-Barre syndrome is an acute demyelinating polyneuropathy disease which is autoimmune in nature and usually follows gastrointestinal or respiratory infections. Dengue fever is however not a common trigger to the condition. Here, we report a patient who developed sensory predominant demyelinating polyradiculopathy during febrile phase of dengue fever. It was later confirmed with serology test and nerve conduction study. He was successfully treated with intravenous immunoglobulin and discharged home well. The purpose of this case report is to highlight that Guillain-Barré syndrome can occur as an uncommon neurological complication of dengue fever which can occur during any phase of the illness.

Introduction

Dengue is a common arboviral infection in the tropical and subtropical country that spread via mosquito bite. It has four serotypes and can cause wide spectrum of clinical manifestations, which ranged from asymptomatic to classical dengue fever, dengue haemorrhagic fever, and dengue shock syndrome [1]. The incidence of dengue fever in Southeast Asia has been high and increasing every year [2]. Neurological manifestations of dengue fever however

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Table 1. Initial blood investigations show leukopenia and thrombocytopenia

Blood parameters	Result	Normal range
Haemoglobin	16.2 g/dL	12–18 g/dL
Platelet	87 × 10^9/L	150–400 × 10^9/L
White blood cell	2.5 × 10^9/L	4.0–11.0 × 10^9/L
Albumin	43 g/L	35–50 g/L
Alkaline phosphatase	141 U/L	50–150 U/L
Alanine transaminase	43 U/L	5–35 U/L
Total bilirubin	8.3 μmol/L	0–13 μmol/L
Creatinine	79 μmol/L	60–120 μmol/L
Sodium	130 mmol/L	135–150 mmol/L
Potassium	4.1 mmol/L	3.5–5.0 mmol/L
Urea	3.9 mmol/L	1.7–8.0 mmol/L
Magnesium	0.9 mmol/L	0.66–1.07 mmol/L
Serum pH	7.45	7.35–7.45
Bicarbonate	24 mmol/L	21–28 mmol/L
Serum lactate	1.0 mmol/L	0.5–2.0 mmol/L
Serum creatine kinase	74 U/L	30–200 U/L

There was mild hyponatremia but otherwise no other electrolyte abnormalities. The alkaline transferase was mildly raised, with normal bilirubin level.

are uncommon. These include encephalitis, aseptic meningitis, transverse myelitis, and Guillain-Barré syndrome (GBS) [3]. In this report, we describe a patient who developed a sensory predominant demyelinating polyradiculopathy disease during the febrile phase of dengue fever. He was successfully treated with intravenous immunoglobulin 0.4 g/kg body weight daily for 5 days. This uncommon complication of a very common infection is the centre of discussion in this case report.

Case Report

A 16-year-old boy with no known medical illness presented on day 4 of dengue fever at febrile phase. The diagnosis of dengue fever was made based on the symptoms, laboratory findings and confirmed with combo test (NS-1 antigen and dengue IgM and IgG antibodies positive). He also complained of recurrent vomiting and colicky abdominal pain for the past 2 days prior to presentation. He denies having any diarrhoea, symptoms of urinary tract infection, or any joint pain. There was no autonomic abnormalities; recurrent vomiting was due to dengue fever. Upon presentation, he has a temperature of 38°C and otherwise his vital signs were stable with the blood pressure of 130/80 mm Hg, pulse rate of 80 beats per minute, and fair perfusion status. On physical examination, he was pink, not jaundice, and mildly dehydrated. His abdomen was soft, not tender, and with no palpable mass or organomegaly. Examination of the cardiorespiratory and central nervous system reveals no obvious abnormality. Blood investigations taken at that time reveal bi-cytopenia, mild transaminitis, and mild hyponatremia (as shown in Table 1), which all are expected from dengue fever. He was given fluid replacement with intravenous 0.9% saline at a rate of 1 mL/kg/h. On day 2 of admission while patient was still in febrile phase, he complained of numbness over the toes

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bilaterally since last night which extended to involve the hindfoot. He has no weakness. Upon examination, it was noted that there was loss of sensation from all modalities over the lower limb up to the level of the knee and also absence of reflexes over both ankles. Pain was not present. Plantar reflexes were muted. Muscle power was full all over the lower limbs and there was no cerebellar sign as well. At this point, acute demyelinating disease involving the sensory nerve was suspected and thus, electrodiagnostic test was done. The nerve conduction studies showed slowing of conduction velocity of sensory potential, normal motor response, and F waves with no increase in distal latency over the common peroneal and posterior tibial nerve. Needle electromyographic examination showed no reduction in distal amplitudes, no positive sharp wave, and no fibrillation potential. These features were suggestive of demyelinating neuropathy. In view of the low platelet count and unable to obtain consent from the patient, lumbar puncture was not performed. However, the serum anti-GM1b antibody level was taken and came back positive. Therefore, he was subjected to intravenous immunoglobulin 0.4 g/kg daily for 5 days with a total dose of 2 g. After completion of the treatment, his sensation and ankle reflexes slowly got back to normal. He was then discharged well and was followed up in the neurology clinic.

Discussion

Dengue is an arboviral infection that is endemic in the tropical and subtropical country. It is considered one of the most common vector-borne viral diseases across the globe. It is transmitted by two species of mosquitos, the *Aedes aegypti* and the *Aedes albopictus*. Dengue viruses belong to the Flaviviridae family and have four serotypes which referred as DEN-1, DEN-2, DEN-3, and DEN-4 [1]. All four serotypes are capable to cause the full spectrum of the disease. The incidence of dengue fever in Malaysia has increased for the last few years, to about 361 cases per 100,000 populations [2]. Dengue fever classically present with fever, joint pains, retro-orbital headaches, skin flush, and morbilliform rashes. In severe cases, it can present as dengue haemorrhagic fever, or dengue shock syndrome. Neurological manifestations of dengue fever however are uncommon, and the incidence has been reported in the medical literature to be only 1–5% [1]. These include encephalitis, encephalopathy, aseptic meningitis, transverse myelitis, and GBS [3].

GBS is a spectrum of disorder which is autoimmune in nature and causes acute inflammatory demyelinating polyradiculopathy. Majority of GBS cases occur 1–3 weeks following an infection, which commonly involve respiratory or gastrointestinal system. Cytomegalovirus, Epstein-Barr virus, *Campylobacter jejuni*, and *Mycoplasma pneumoniae* are among the commonly identified precipitating infective agents [3]. Dengue virus however is not a common trigger. The mechanism on how dengue virus triggers GBS is still not well understood. But the molecular mimicry that triggers immunological response which involves pro-inflammatory cytokines like TNF-α, interleukins, and complements that targets the myelin and axons are postulated as possible mechanisms [4].

GBS is diagnosed clinically based on the recognition of particular pattern of muscle weakness which is bilateral, ascending in nature, and associated with absence of reflexes. Investigations are helpful to support the diagnosis, which include cerebrospinal fluid analysis, nerve conduction study (NCS), and serum autoantibody level, like anti-GM1b antibody. The distinctive cerebrospinal fluid finding is increased protein level without accompanying pleocytosis, a phenomenon which is called albuminocytologic dissociation. NCS will show pattern of demyelinating neuropathy, which include delayed conduction velocity, conduction block, prolonged distal latency, prolonged F wave latencies, and reduced amplitude of compound muscle action potentials [5]. Although the classic presentation of GBS is symmetrical progressive

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motor weakness and sensory involvement, the possibility of an acute sensory neuropathy variant of GBS has been reported in small number in the literature [6, 7]. It was described by Oh et al. [6] as an acute, monophasic, and generalized neuropathy characterized clinically by exclusively sensory symptoms. Uncini and Yuki [7] have suggested the classification of sensory GBS and its related disorders into three categories: acute sensory demyelinating polyneuropathy, acute sensory large fibre axonopathy ganglionopathy, and acute sensory small fibre neuropathy ganglionopathy. The presence of autoantibody against ganglioside, such as anti-GM1 antibodies, is usually found and can be used to support the diagnosis of GBS. Although it is more common in the axonal variant of GBS, it is present in 12–25% of cases of acute inflammatory demyelinating polyneuropathy [8].

Treatment should be initiated as soon as possible after the diagnosis is made, which involves high dose intravenous immunoglobulin (IVIg) 2 g/kg body weight divided in 5 daily doses or plasmapheresis. Both of these treatment modalities are equally effective for typical GBS. Glucocorticoids have been found to be not effective in treatment of GBS [9].

Our patient presented at the febrile phase of dengue fever with subtle symptoms of lower limb numbness which progresses from the toes and then involves the whole foot. Upon examination, the ankle and knee reflexes were diminished which give the impression of GBS. NCS revealed abnormal sensory potentials with normal motor potentials which are suggestive of sensory predominant GBS. EMG did not show any denervation pattern. This makes the case unique as to the extent of our knowledge, and it is the first case of sensory predominant GBS that occurs concomitantly with dengue infection. The patient responded well to IVIg therapy with good recovery.

Conclusion

In conclusion, this case report serves to remind that GBS can occur as a neurological complication of dengue infection. This condition is generally underestimated and should always be considered if a patient of dengue fever develops progressive weakness of the limbs and treatment should be initiated as early after diagnosis as possible.

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Statement of Ethics

This study protocol was reviewed and the need for approval was waived by the Ethical Committee from Hospital Canselor Tuanku Muhriz. Written informed consent was obtained from the parents of the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

We declare there is no conflict of interest with regard to the publication of this case report.

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Author Contributions

Alvin Oliver Payus: manuscript writing, final editing, and corresponding author. Azliza Ibrahim: data collection and manuscript writing. Constance Liew Sat Lin: manuscript writing and final editing. Tan Hui Jan: final editing and supervisor.

Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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