Imtiaz *et al.*
Egypt J Neurol Psychiatry Neurosurg (2023) 59:149
https://doi.org/10.1186/s41983-023-00741-4

The Egyptian Journal of Neurology, Psychiatry and Neurosurgery

CASE REPORT

Open Access

Dengue-induced Guillain–Barre syndrome: a case series

Hina Imtiaz[1*], Ayisha Farooq Khan[1] and Sara Khan[1]

Abstract

Background Dengue virus is an RNA virus that is associated with a myriad of neurological manifestations. Less than 5% of patients develop neuromuscular complications. Guillain–Barre syndrome (GBS) is an uncommon neurological sequelae of dengue fever. Studies have shown acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN) to be the most common variants associated with dengue fever in Asian countries. Very few cases have been reported from Pakistan to date.

Case presentation We present four adult patients with dengue-associated GBS. The time interval between onset of symptoms of dengue fever and development of lower limb weakness in all patients was between 6 and 20 days. Dengue was diagnosed based on either serology or dengue NS1 antigen testing. Acute inflammatory demyelinating polyneuropathy (AIDP) ($n=1$), AMAN ($n=1$), and AMSAN ($n=2$) variants were identified. One patient had a coexisting myopathy which has not been previously reported. All patients showed good recovery after treatment with plasmapheresis or intravenous immunoglobulins.

Conclusions Our case series is valuable in contributing to the limited pool of reported cases of dengue fever complicated by GBS. Early detection of new onset symmetrical limb weakness during or after a dengue infection is imperative for early treatment and to limit disability.

Keywords Dengue virus, Guillain–Barre syndrome, Plasmapheresis, Intravenous immunoglobulin, Acute inflammatory demyelinating polyneuropathy

Background

Dengue fever is an infection caused by the dengue virus, which is a single stranded RNA virus belonging to the Flaviviridae family. While most cases of dengue fever present with mild symptoms, such as fever, headache, and joint pain, a small percentage of patients can develop more severe manifestations. Neurological complications are reported to occur in less than 5% with dengue fever [1]. These may include encephalitis, aseptic meningitis, intracranial haemorrhage, myelitis, mononeuropathies, polyneuropathies, brachial plexopathies, and Guillain–Barre syndrome (GBS). GBS is a post infectious ascending, polyradiculoneuropathy accompanied by areflexia, motor paralysis, and elevated cerebrospinal fluid (CSF) total protein without raised cell counts [2].

Although the precise mechanism through which the dengue virus triggers GBS is not completely understood, it is hypothesized that the virus may induce the production of antibodies that attack peripheral nerves, resulting in limb weakness and paralysis [3]. Substances with pro-inflammatory properties that are involved in the immune response to dengue virus (DENV), such as tumor necrosis factor (TNF), interleukins, and complements, may play a significant role in the development of GBS [4].

In Asian countries, the axonal variant of GBS is frequently observed, while the demyelinating variant is more prevalent in Western countries [5]. Limited reports

*Correspondence:
Hina Imtiaz
hina.imtiaz@aku.edu
[1] Section of Neurology, Department of Medicine, Aga Khan University, National Stadium Road, Karachi, Pakistan

exist in literature documenting GBS cases in adults with dengue fever [6, 7]. In all reported cases, onset of GBS symptoms occurred after recovery from the initial dengue infection. The specific variants of dengue that can cause GBS are unknown.

Herein, we report four cases of GBS variants associated with dengue virus and their outcomes.

Case presentation

Case 1

A 35-year-old male, with no known comorbid, presented with complaints of pain and weakness in both lower limbs for the past 5 days. He had a fever 12 days ago that lasted for 5 days and had diarrhea 7 days prior to his presentation. On arrival, he was cognitively intact, with normal vitals. Dengue NS 1 antigen testing was positive. Pertinent findings on neuromuscular examination included muscle strength of Medical Research Council (MRC) grade 3/5 in lower limbs, both proximally and distally, and 5/5 in the upper limbs. Reflexes were absent with flexor planter responses. No sensory loss was identified. Cranial nerves were intact and cerebellar exam was also unremarkable. Electromyography/nerve conduction studies (EMG/NCS) revealed findings consistent with a severe non irritable myopathy affecting upper and lower extremities along with an acute demyelinating polyradiculoneuropathy (AIDP) variant of GBS. The patient was advised treatment, but he left against medical advice due to financial reasons.

Case 2

A 69-year-old male, with no previous medical conditions, presented to the emergency department with complaints of high-grade fever and lower back ache for 10 days and weakness in the lower limbs for 5 days. On arrival, he was alert, and well-oriented. Vitals were within normal range. Neurological exam revealed powers of 3/5 in the lower limbs and 4/5 in the upper limbs, both proximally and distally. Reflexes were + 1 and planters were flexor in response bilaterally. Sensory exam was unremarkable and cranial nerves were also intact. Single breath count was 18. EMG/NCS revealed findings consistent with an acute sensorimotor axonal polyneuropathy (AMSAN) affecting upper and lower extremities. Dengue IgM serology was positive. Patient was treated with five sessions of plasmapheresis and his powers improved to 4/5 in the lower limbs and + 4/5 in the upper limbs.

Case 3

A 21-year-old male presented to the emergency department with fever and generalized body aches for 12 days with bilateral upper and lower limb weakness for 3 days. Dengue NS 1 antigen was positive. On arrival, his vitals were within normal limits. Higher mental functions were intact and pertinent findings on neuromuscular examination revealed powers of 2/5 in both upper limbs and 1/5 in the lower limbs along with absent reflexes. Cranial nerves and sensory exam was unremarkable. Forced vital capacity was 1.6 L. Based on EMG/NCS testing, the patient was diagnosed with an acute motor axonal neuropathy (AMAN) variant of GBS. The patient received five sessions of plasmapheresis, which resulted in an improvement in muscle strength to a grade of 3/5 in both upper and lower limbs at discharge from hospital.

Case 4

A 46-year-old male presented with the complaint of fever one month ago lasting for few days, and ascending weakness for 20 days. On examination, he was awake, alert, and following commands. Vitals revealed a blood pressure of 110/70 mm Hg, pulse of 70/min, regular, and respiratory rate of 18 breaths/min. His extraocular movements and facial nerve exam was intact. Motor examination showed powers of 2/5 in the lower limbs and 3/5 in the upper limbs with no sensory deficits identified. Reflexes were absent. Single breath count was 12, and forced vital capacity was 1.3 L. EMG/NCS showed findings consistent with an AMSAN variant of GBS. His Dengue IGM was positive. The patient received 5 doses of IVIG. But subsequently, he developed hypoxic respiratory failure secondary to pneumonia, and ultimately required intubation. Two days later, the patient developed an inferior wall myocardial infarction, followed by cardiac arrest resulting in expiration.

Conclusion

The dengue virus, commonly referred to as DENV, has four serotypes: DENV1, DENV2, DENV3, and DENV4. Each of these serotypes can result in a wide range of illness, ranging from subclinical infection to mild, self-limiting dengue fever, as well as severe and potentially fatal conditions such as dengue haemorrhagic fever/dengue shock syndrome [8]. All the patients described in our case series were male, with ages ranging from 21 to 69 years They all presented within three weeks of contracting dengue fever, which was confirmed by either NS1 antigen or IgM serology testing. Given the endemic nature of dengue in our region, we routinely screen patients for dengue with high grade fever, with or without a low platelet count. One patient was diagnosed with AIDP, another with AMAN, and two with AMSAN based on electrophysiological testing. Table 1 provides a summary of the cases.

Lumbar puncture was not performed in any of these patients. Notably, the patient diagnosed with AIDP also had a myopathy, which is a unique finding as there have

Table 1 Demographic details of our patients

	Case 1	Case 2	Case 3	Case 4
Gender/age	M/36	M/21	M/69	M/45
Comorbid conditions	None	None	None	Diabetes Mellitus
Symptoms	Fever—12 days ago Bilateral lower limb weakness—5 days	Fever and body aches-10 days Bilateral lower limb weakness—5 days	Fever—12 days Bilateral limb weakness-3 days	Fever—1 month ago Ascending weakness—20 days
CNS Motor examination	Powers: 3/5 lower limbs 5/5 upper limbs Areflexia	Powers: 3/5 lower limbs 4/5 upper limbs Reflexes: + 1	Powers: 1/5 lower limbs 2/5 upper limbs Areflexia	Powers: 2/5 lower limbs 3/5 upper limbs Areflexia
Evidence of dengue	NS1 antigen positive	Dengue IgM positive	Dengue NS1 antigen positive	Dengue IgM positive
Platelets on admission (*10E9/L) (Normal Range: 154–433)	224	151	306	160
CPK Levels (U/L)	62	Not done	Not done	Not done
EMG/NCS findings	Non-irritable myopathy affecting upper and lower extremities AIDP	AMAN	AMSAN	AMSAN
Treatment received	Left the hospital against medical advice Received plasmapheresis 5 sessions at another hospital	5 sessions of plasmapheresis	5 sessions of plasmapheresis	Expired. Five doses of IVIG
Outcome at 3 months discharge	Improved. Now able to walk independently	Improved. Able to walk independently	Improved. Now able to walk with one person support	No improvement. Passed away secondary to cardiac arrest and underlying sepsis

been no reports of both conditions coexisting after dengue. It is to be noted that the myopathy was non-irritable, accompanied by a normal CPK level, suggesting a non-inflammatory cause. This could be due to a latent underlying myopathy or possibly related to dengue fever. It is worth considering that the study might have been conducted prematurely in the course of the disease, or this myopathy might stem from an existing underlying incidental myopathy. Unfortunately, this patient left the hospital against medical advice without receiving any treatment, and as a result, the outcome of illness is unknown. Two of the patients with AMAN and AMSAN variant showed improvement after receiving plasmapheresis and IVIG treatment respectively (the decision to receive IVIG or plasmapheresis was based on patient's preference). However, one patient with AMSAN experienced respiratory failure due to hospital-acquired pneumonia and required intubation. He had a cardiac arrest and ultimately passed away.

In a review by Garg et al., which included 29 patients with dengue fever associated GBS, it was reported that most patients had a low platelet count at the time of developing weakness, indicating that GBS was a manifestation of acute dengue fever [1]. On the contrary, our patients had a normal platelet count, suggesting that the acute neuropathy came in the aftermath of acute viremia and not during it. This suggests that the relationship between dengue fever, GBS, and platelet counts may not be straightforward and requires further investigation. It should be noted that variants of dengue are not tested for routinely; therefore, it is not clear if a certain variant of dengue is associated more with the development of GBS.

The outlook of GBS is favorable. A study conducted on ten patients in Brazil with GBS following dengue fever revealed that all patients achieved full recovery after receiving IVIG treatment, and most of them showed recovery within 3 months. AMSAN variant was identified in all these cases [9]. In our series, patient with AMSAN variant had a more severe phenotype and lack of response to appropriate treatment. While the prognosis of GBS is typically good, patients with severe disease may have a mortality rate of around 10%, particularly when they experience complications from extended mechanical ventilation [10]. Three of our patients at 3 months follow up were ambulatory.

Overall, our case series adds to the growing body of evidence that dengue fever can trigger GBS, with various clinical variants observed. The absence of low platelet counts (Refer to Table 1 for laboratory details) in our patient raises questions about the underlying

mechanisms of this association and highlights the need for further studies. It is also important to note that while most of the patients recover from illness, some of them may have a poor prognosis despite timely intervention. Therefore, a multidisciplinary approach and close monitoring of patients with dengue associated GBS are crucial for achieving the best possible outcomes.

Dengue fever is a significant public health concern worldwide, particularly in endemic areas. While uncommon, GBS should be considered as a potential diagnosis in patients who experience weakness following dengue infection. In developing nations where such cases may be under-reported, recognizing this condition is crucial in reducing its associated morbidity and mortality.

Abbreviations

AIDP	Acute inflammatory demyelinating polyneuropathy
AMAN	Acute motor axonal neuropathy
AMSAN	Acute motor sensory axonal neuropathy
CNS	Central nervous system
CPK	Creatine phosphokinase
CSF	Cerebrospinal fluid
DENV	Dengue virus
EMG/NCS	Electromyography/nerve conduction studies
GBS	Guillain–Barré syndrome
IgM	Immunoglobulin M
IVIG	Intravenous immunoglobulin
MRC	Medical Research Council
NS 1	Nonstructural protein 1 antigen
RNA	Ribonucleic acid
TNF	Tumor necrosis factor

Acknowledgements
The authors would like to acknowledge Dr. Dureshahwar Kanwar for helping us with the interpretation of the EMG/NCS.

Author contributions
HI and AK wrote the manuscript; HI, AK and SS contributed significantly to analysis and manuscript preparation; HI, AK, and SS contributed to the conception of the study. The authors have read and approved the manuscript.

Funding
No funding was obtained for this article.

Availability of data and materials
The authors confirm that the data supporting the findings of this study are available within the article.

Declarations

Ethics approval and consent to participate
Need for approval was waived by the ethical research committee.

Consent for publication
Written informed consent was obtained from the patients for publication of this case report and any accompanying images.

Competing interests
The authors declare that they have no competing interests.

Received: 15 June 2023 Accepted: 20 October 2023
Published online: 08 November 2023

References

1. Garg RK, Malhotra HS, Jain A, Malhotra KP. Dengue-associated neuromuscular complications. Neurol India. 2015;63:497.
2. Puah SH, Chang CY, Steven A. Guillain–Barre Syndrome complicating dengue fever: a case report. 19th International Congress on Infectious Diseases. 2020. https://doi.org/10.13140/RG.2.2.11001.08807
3. Jasti AK, Selmi C, Sarmiento-Monroy JC, Vega DA, Anaya JM, Gershwin ME. Guillain–Barré syndrome: causes, immunopathogenic mechanisms and treatment. Expert Rev Clin Immunol. 2016;12:1175–89.
4. Ralapanawa DM, Kularatne SA, Jayalath WA. Guillain–Barre syndrome following dengue fever and literature review. BMC Res Notes. 2015;8:1–5.
5. Prado MB Jr, Narito KM, Adiao KJ. Anti-GM1 IgM antibody positive axonal variant of Guillain-Barre-syndrome in a pediatric patient with dengue fever. J Neuroimmunol. 2021;355: 577572.
6. Chew NK, Goh KJ, Omar S, Tan CT. Guillain–Barre syndrome with antecedent dengue infection: a report of two cases. Neurol J Southeast Asia. 1998;3:85–6.
7. Qureshi NK, Begum A, Saha PR, Hossain MI. Guillain–Barre syndrome following dengue fever in adult patient. J Med. 2012;13:246–9.
8. Martina BE, Koraka P, Osterhaus AD. Dengue virus pathogenesis: an integrated view. Clin Microbiol Rev. 2009;22:564–81.
9. Fragoso YD, Gomes S, Brooks JB, Matta AP, Ruocco HH, Tauil CB, et al. Guillain–Barré syndrome and dengue fever: report on ten new cases in Brazil. Arq Neuropsiquiatr. 2016;74:1039–40.
10. Boo YL, Aris MA, Chin PW, Sulaiman WA, Basri H, Hoo FK. Guillain–Barré syndrome complicating dengue fever: two case reports. Tzu Chi Med J. 2016;28:157–9.

Publisher's Note