Case Report

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An unusual case of acute motor axonal neuropathy (AMAN) complicating dengue fever

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SUMMARY Neurological complications are increasingly being reported in dengue fever, and the dengue virus is now recognized as a neurotrophic virus. The damage caused by inflammatory cytokines in the febrile phase and molecular mimicry in the recovery phase is responsible for these neurological manifestations. We report such an unusual neurological complication occurring in a 27-year-old female in the recovery phase of dengue fever, who developed an acute onset of ascending symmetric weakness of all four limbs without any sensory, autonomic, cerebellar, or cranial nerve involvement. She was diagnosed as having an acute motor axonal neuropathy (AMAN) variant of Guillain-Barre syndrome (GBS) based on a nerve conduction study (NCS) showing axonal neuropathy and contrast-enhanced magnetic resonance imaging (CE-MRI) showing root enhancement at the region of the cauda equina. She was treated with intravenous immunoglobulin (IVIG) and showed full recovery from symptoms with treatment. Our case highlights the importance of being aware of such rare neurological complications in dengue fever. Early detection and rapid initiation of treatment can lead to the complete reversal of neurological deficits.

Keywords Guillain-Barre syndrome, intravenous immunoglobulin, demyelination, dengue fever, nerve conduction study

1. Introduction

Dengue virus is now known to be a neurotropic virus, and neurological complications are being increasingly reported in dengue fever. The damage caused by inflammatory cytokines in the febrile phase and molecular mimicry in the recovery phase are responsible for these neurological manifestations. Encephalitis, myelitis, myositis, Guillain-Barre syndrome (GBS), hypokalemic periodic paralysis have been reported in dengue fever. We report an unusual case of a 27-year-old female, in the recovery phase of dengue fever, who presented with acute onset of ascending symmetric weakness of all four limbs, diagnosed as acute motor axonal neuropathy (AMAN) variant of GBS based on nerve conduction study (NCS) showing axonal neuropathy and contrast-enhanced magnetic resonance imaging (CE-MRI) showing root enhancement at the region of cauda equina. She was treated with intravenous immunoglobulin (IVIG) and showed full recovery from symptoms with treatment.

2. Case Report

A 27-year-old female with no comorbidities presented with acute onset weakness of all four limbs. Weakness started in the lower limbs and progressed to the upper limbs after 24 hours. Weakness in the lower limbs involved the distal muscles in the form of difficulty in wearing footwear and proximal muscles in the form of difficulty in walking, standing up from a sitting position, and climbing stairs. Upper limb weakness was more distal in the form of difficulty holding a pen, weak handgrip and difficulty in braiding hair. There was no history suggestive of any cranial nerve involvement like drooping of eyelids, diplopia, deviation of tongue or angle of mouth. There were no associated sensory symptoms like numbness or paraesthesia. There was no associated headache, memory loss, behavioural abnormalities, abnormal movements or vomiting. There was no associated bowel or bladder involvement. There was no associated shortness of breath suggestive of diaphragmatic weakness. There was no history of recent

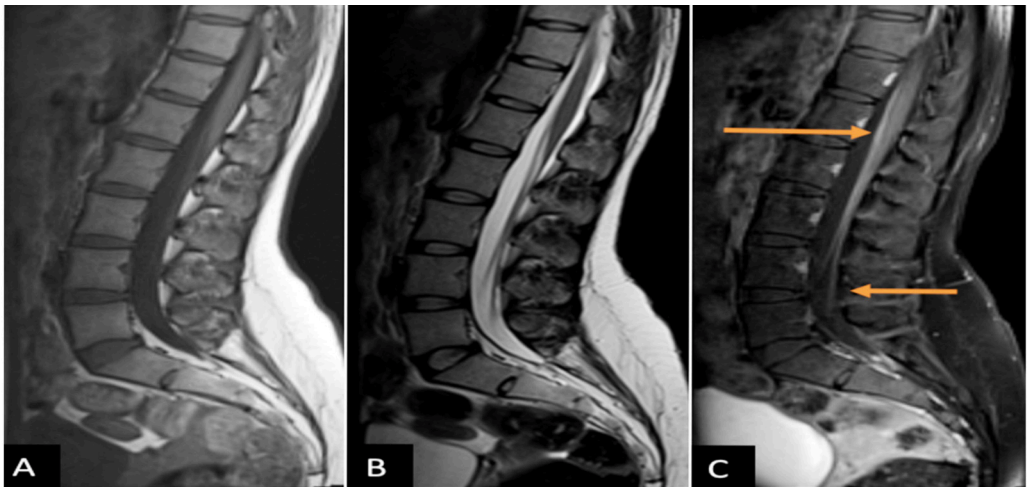

Figure 1. Arachnoiditis. Sagittal MRI images of the lumbar spine, T1w (A), T2w (B), Post-contrast (C) show thickening and enhancement of the thecal sac and the Cauda equina nerve roots (arrow).

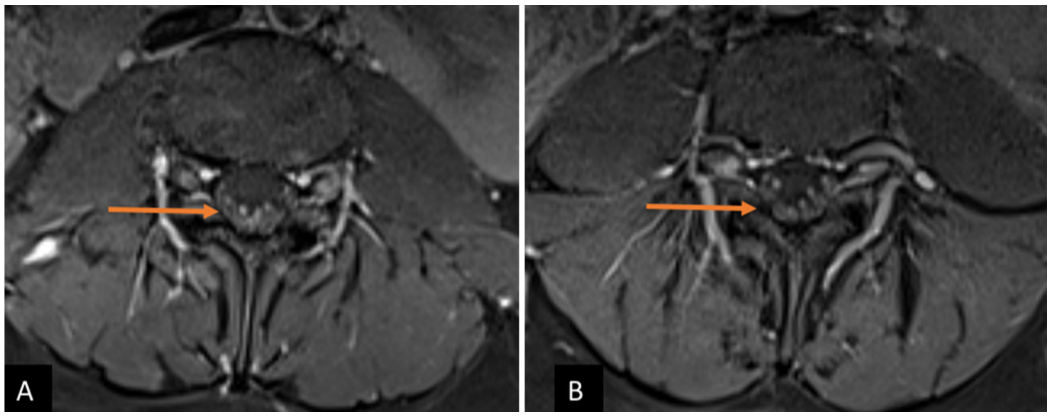

Figure 2. Arachnoiditis. Axial post contrast MRI images (A, B) of the lumbar spine, show posterior layering with thickening and enhancement of the lumbar nerve roots (arrow).

vaccination before the onset of weakness. There was no history of recent diarrhoeal or respiratory disease.

A week before the onset of weakness, she had a high-grade fever for 2 days associated with calf muscle pain and blanching rashes over arms and neck. She tested positive for NS1 antigen and was diagnosed as having dengue fever without warning signs.

At presentation, she was conscious, oriented to time, place, person and cooperative. Her pulse rate was 78 bpm and blood pressure was within normal limits. She was not tachypneic, had room air saturation of 98% and single breath count of 36. Examination of the nervous system revealed symmetric lower motor neuron type of weakness involving all four limbs. She had a power of 4+/5 at shoulder joint; 4-/5 at the elbow, wrist; 4-/5 at the hip, knee; 3/5 at the ankle joint, with normal bulk and generalised hypotonia. All deep tendon reflexes were preserved and Babinski response was negative.

Given the acute onset of ascending, symmetric lower motor type of weakness involving all limbs, a provisional diagnosis of GBS was made. Other possible differentials kept were acute porphyria and lead intoxication.

Routine blood investigations showed a normal leukocyte count of 5,110 cells/uL with 63.2% neutrophils, mild anaemia (haemoglobin 10.8 g/dL) secondary to folate deficiency and normal platelet counts. Hepatic and renal functions were within normal limits. Creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) levels were within normal limits. NCS showed reduced compound muscle action potential (CMAP) in bilateral median and ulnar, left tibial and right peroneal nerves; unrecordable CMAPs in the right tibial and left peroneal nerves and normal F waves. CE-MRI of brain and spine showed nerve root enhancement in the cauda equina. Lumbar puncture was deferred as the patient was in the initial week of illness.

A diagnosis of AMAN variant of GBS was made and the patient was started on IVIG 2 g/kg given over 5 days. By day 3 of treatment, the patient reported modest improvement in symptoms and she was discharged after the course of IVIG. At the time of discharge, power was 5/5 in all joints of upper and lower limbs, except the ankle joint where the power was 4-/5. The patient was closely followed up on OPD basis and gradually power at the ankle joint also returned to normal.

3. Discussion

Sanguansermsri in 1976 first reported neurological complications in dengue fever (DF) (*1*). Initially believed to be a non-neurotrophic virus, today there is enough evidence to suggest that dengue virus is neurovirulent. Viral proteins, RNA and antibodies directed against dengue virus have been detected in cerebral-spinal fluid (CSF). Dengue virus 2 and 3 are more likely to cause neurological complications (*2*).

Hendarto *et al*. reported the incidence of neurological complications in dengue fever as 0.5-6% (*3*). In dengue endemic countries like Brazil, neurological complications have been reported in as high as 21% of dengue cases (*4*). Koshy *et al*. conducted a prospective study in north west India to identify the prevalence of neurological manifestations in dengue fever. 799 dengue patients during the epidemic of 2010 were screened for neurological manifestations and it was present in 21 patients (2.63%) (*5*). Neurologic manifestations are so prevalent in some endemic areas such that in patients presenting with acute flaccid paralysis, dengue viral infection must be ruled out as a cause. World Health Organisation (WHO), in the 2009 classification of DF, has categorised the presence of neurological complications as severe dengue (*6*).

Nervous system involvement has been reported in both the febrile phase as well as in the convalescence phase. Damage caused by pro-inflammatory cytokines like tumour necrosis factor (TNF), interleukins, complements and molecular mimicry in the form of the immune response to the dengue virus antigens that have been misdirected against the host nerve tissue are believed to be the plausible cause in the febrile phase and recovery phase respectively. Higher body temperatures, presence of severe thrombocytopenia, transaminitis and rashes, hemoconcentration are risk factors for neurological complications (*7*).

Verma *et al*. and Murthy, Marzia and colleagues classified neurological complications of dengue fever into (a) neurotrophic complications like encephalitis, myelitis, myositis; (b) systemic complications like hypokalemic periodic paralysis; and (c) post-infectious immune mediated complications like GBS, acute disseminated encephalomyelitis (ADEM), opsoclonus myoclonus syndrome, neuromyelitis optica (NMO) (*8-10*). Solbrig *et al*. proposed a different classification system: (a) involvement of central nervous system and eyes, (b) peripheral nervous system and (c) post dengue immune mediated syndromes (*11*). Peripheral nervous system manifestations contribute to 5% of neurological manifestations of DF (*12*).

GBS affecting dengue patients is being increasingly reported now. Tan *et al*. in 2019 published a study evaluating 95 patients admitted with GBS between 2010 and 2018 at a tertiary care centre in Kaula Lampur. Sera of these patients were tested for IgM antibodies against cytomegalovirus (CMV), Ebstein Barr virus (EBV), dengue, mycoplasma pneumoniae and IgG antibodies against *Clostridium jejuni*. Twenty percent of the patients were positive for dengue IgM antibodies and this was statistically significant (p value = 0.034) and dengue related GBS was more likely to have diarrhoea, facial palsy and more severe neurological deficit (*13*). GBS is more likely to occur early in the course of dengue fever. Average time between onset of fever and neurological deficit was 2 days (*14*).

Our patient presented with symptoms suggestive of AMAN in the recovery phase of dengue fever. She was treated with IVIG 2 g/kg given over five days and started showing improvement in weakness by day 3 of IVIG. Treatment response with both IVIG and plasmapheresis are equivalent and there is no extra benefit from combining the two modalities of treatment (*15*). When the patient was followed up a month after discharge, she had recovered completely from the neurological deficit.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

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