Dengue infection and Guillain-barre syndrome

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Abstract
Guillain-barre syndrome (GBS) following dengue infection is quite rare. This case report presents a patient with acute onset quadriparesis, bilateral facial nerve palsy and bulbar involvement associated with the dengue virus infection without any typical symptoms of dengue fever. Clinicians should always keep this association in mind when a patient presents with acute ascending weakness of limbs in the endemic areas even if the patient does not have symptoms suggestive of dengue, because a large number of dengue infections may be asymptomatic.

Keywords: Dengue, neurology, AIDP, guillain-barre syndrome

Introduction
Guillain-barre syndrome (GBS) or acute inflammatory demyelinating polyneuropathy (AIDP) is a rapidly ascending motor paralysis associated with areflexia and CSF albumino-cytological dissociation [1]. GBS is mostly associated with infections like Campylobacter jejuni, Cytomegalovirus, Epstein-Barr virus and HIV even though the exact cause remains unknown. Dengue is an arboviral infection with 390 million infections occurring annually. It is endemic in more than 100 countries involving America, Western Pacific regions and South-East Asia which is more seriously affected. Asia represents 70% of the global burden of disease [2]. It manifests typically ranging from mild fever to severe dengue including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), requiring hospitalization. Neurological manifestations like meningitis, encephalitis and myelitis may be associated with acute infection, and Bell's palsy, psychosis, acute disseminated encephalomyelitis, epilepsy and even dementia have been reported as post-infectious sequelae [3]. GBS is rarely seen in dengue. Here we present a case report of GBS secondary to dengue infection without any typical symptoms of dengue infection.

Materials and Methods
A 48-year gentleman, a mason by occupation, presented with weakness of bilateral lower limbs for two days which progressed to involve bilateral upper limbs and inability to lift his head off the pillow. The patient also had a difficulty in swallowing both solids and liquids, inability to close both his eyes and drooling of saliva. There was no history of sensory loss or bowel and bladder dysfunction. There was a history of fever with myalgia 3 weeks back for which he took over-the-counter medications and symptomatically improved. There was no history of diarrhea, respiratory illness or recent vaccination before the illness. He was a diagnosed hypertensive for 5 years being treated with tablet amlodipine 5mg q24h. On examination, the patient was conscious and oriented with normal vital parameters. Neurological examination showed bilateral LMN facial nerve palsy with a diminished gag reflex and inability to lift up his head from the pillow. Further, power was 2/5 in both upper limbs and 1/5 in both lower limbs at all joints with absent deep tendon and plantar reflexes. Sensory examination was within normal limits. The rest of the systemic examination was normal. A provisional diagnosis of Guillain-Barre syndrome with facial nerve palsy and bulbar involvement was considered. His hemogram was suggestive of anemia (Hb of 8 g%). Peripheral blood smear showed normocytic normochromic to microcytic hypochromic RBCs. Kidney function tests, liver function tests and serum electrolytes were within normal limits. Iron studies were suggestive of iron deficiency anemia. Serum globulin levels were increased with an A: G ratio of 1:1.6, however, serum protein electrophoresis was normal. Stool microscopy and fecal occult blood test were negative. CSF study showed albumin-cytological dissociation (absent cells with sugar 98 mg/dl and protein 325 mg/dl). Nerve conduction studies revealed delayed nerve conduction velocity in the median, ulnar and tibial nerves with prolonged distal latency, low amplitude in peroneal nerve, F waves were absent, suggesting demyelinating neuropathy. Sugar profile and vitamin B12 levels were normal. HIV, hepatitis B and C serology, and SARS-CoV-2 RT PCR were negative. His Dengue IgM serology was positive. The patient was diagnosed with GBS secondary to dengue infection and was given Intravenous immunoglobulins (IVIGs) at a dose of 20 g/day based on the 0.4g/kg/day regime. On the third day, the patient was able to lift his head off the pillow, was able to close both the eyelids and his gag reflex returned. Power of the upper limb improved to 4/5 and the lower limb to 2/5 on the fifth day. At discharge, the patient was advised regular limb physiotherapy and neurology clinic follow-up.
Discussion

Dengue is an arbovirus belonging to the family Flaviviridae. Dengue infection causes a varied spectrum of presentations including asymptomatic and mild fever to as severe as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). We describe this case of GBS associated with dengue without any typical symptoms of dengue infection. In a study by Bhushan et al., 14.6% of the confirmed dengue cases had a systemic neurological complication (4). Neurological complications in dengue as proposed by Murthy et al. are classified as follows:

1. Direct neurotropic complications such as encephalitis and myositis
2. Systemic neurological complications including encephalopathy, cerebrovascular complications due to thrombocytopenia and metabolic complications such as hypokalemic paralysis
3. Immune-mediated neurological complications included acute disseminated encephalomyelitis (ADEM), Guillain-Barre syndrome (GBS), and opsoclonus myoclonus syndrome (OMS)

According to Bhushan et al., GBS with dengue infection is seen in severe dengue syndrome. However, Soares et al. reported a case series of seven dengue IgM positive patients with GBS in which 4 patients had mild symptoms, 2 patients denied any infectious symptoms and among seven, only one had typical symptoms for dengue. All the reported cases had the onset of weakness after recovery from the initial dengue infection. Our patient had no classical symptoms of dengue fever. The mechanism for dengue-associated GBS is likely due to immune-mediated neurological disease [4]. Dengue infections have abnormal immune responses including cytokine and chemokine activation. Dengue patients produce non-structural protein 1 antibody (anti-NS1) which cross-reacts with platelets and endothelial cells. This autoimmune response may be involved in the development of neurological complications [5]. Our patient was treated with intravenous immunoglobulins 20g/day for 5 days. Studies showed IVIG is equally effective as plasma exchange with lesser side effects [6]. The response to IVIG treatment for GBS is highly variable. The Independent predictors for poor responsiveness to IVIG are disease severity at presentation, age above 40yrs and peroneal nerve conduction block [7]. Our patient, aged 48 years, presented with acute onset areflexic quadripareisis, bilateral LMN facial nerve palsy, neck and bulbar muscles involvement with nerve conduction study showing peroneal nerve conduction block which may be some of the reasons for the partial response to IVIG treatment.

Conclusion

Guillain-Barre syndrome secondary to dengue infection is rare. GBS can be seen even if there are no typical symptoms of dengue infection. GBS should be diagnosed clinically along with findings on nerve conduction studies, and intravenous immunoglobulin or plasma exchange should be initiated early, for a better prognosis. Clinicians should always keep the possibility of subclinical dengue infections in a patient of GBS residing in endemic countries.

Declaration of Patient Consent

We have obtained written consent from the patient before the submission of this case report.