

Guillain-Barre Syndrome following Dengue Fever: Report of 3 Cases

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Guillain-Barre syndrome is a post infectious polyradiculoneuropathy. It is equally prevalent in both the adult and the pediatric populations. Guillain-Barre syndrome following dengue fever is not a classically described entity and has not been reported in children.

Key words: *Dengue fever, Demyelination, Guillain-Barre syndrome.*

Guillain-Barre syndrome is a post infectious polyradiculoneuropathy. It is equally prevalent in both the adult and the pediatric populations. The classical agents that have been known to cause Guillain-Barre syndrome are gastrointestinal infection with campylobacter jejuni and respiratory infections caused by mycoplasma. The other agents implicated in Guillain-Barre syndrome are cytomegalovirus, Ebstein-barr virus and the herpes virus. Here we are reporting 3 cases of Guillain-Barre syndrome following dengue fever.

Case Report 1

A 2½-year-old girl with normal

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development presented with progressive weakness of lower limbs which at the time of presentation involved the upper limbs as well. There was no history of seizures or loss of consciousness. Two weeks prior to the illness the child had a bout of high-grade fever and myalgia associated with headache and vomiting. The local physician noticed a rash over the face and trunk. The complaints subsided with conservative management at the local hospital.

On examination the child was conscious and well oriented. The tone was decreased in all the four limbs. The lower limbs had lesser power when compared to the upper limbs, the proximal muscles in both the upper and lower limbs were weaker. The neck and trunk muscles were also involved. The deep tendon reflexes were absent. The cranial nerves were spared. Other systems were within normal limits. The case was reported as an acute flaccid paralysis.

Lumbar puncture done at the time showed 10 lymphocytes per cubic milli meter and a raised protein level of 150 mg/dL. The nerve conduction velocities showed slowing of the distal latencies with the absence of the F wave. The stool sample sent for investigation of acute flaccid paralysis was negative for the polio virus. The IgM antibody for the dengue virus was strongly positive. The culture of the spinal fluid was sterile. The child was treated with intravenous gammaglobulin. The recovery was complete in three weeks.

Case Report 2

The second child, presented on the same day, was an 8-year-old girl with repeated episodes of tripping of an acute onset, with an inability to lift her hands above the head. As the disease progressed the child could not sit up in bed. There was an alteration of voice associated with difficulty in swallowing. The

child also complained of pain in the thigh and calf. Ten days prior to this, the child attended the local hospital outpatient with fever and a generalised rash. The symptoms were not associated with coryza but had arthralgia and headache. The complaints subsided in a few days.

Examination revealed a child with normal sensorium. There was bilateral palatal weakness and a bilateral lower motor neuron facial nerve weakness. There was hypotonia of both the upper and lower limbs. There was grade two power in the lower limbs with grade three power in the upper limbs. The deep tendon reflexes could not be elicited. There was no sensory or bladder involvement. The other systems were within normal limits.

Lumbar puncture showed no abnormality. The culture of the spinal fluid was sterile. The nerve conduction velocity in the upper limb was 24m/sec and in the lower limb was 15m/sec. There was absence of the F wave. The packed cell volume and the platelet count were within the normal limits. Imaging studies of the brain were within normal limits. The study for viral markers showed markedly elevated titres of IgM antibody against the dengue virus. Stool samples were negative for the poliovirus. The child responded to intravenous gammaglobulin.

Case Report 3

The third child one and half years old presented to us with an inability to stand. With the onset of illness initially there was an inability to stand. Later she could not sit up. Two weeks earlier the child had high-grade fever with mild facial puffness. Investigation then revealed raised IgM antibody to the dengue virus.

The child was conscious and alert. The palatal movements were sluggish. There was

loss of head control with flaccid weakness of all limbs. The reflexes were absent. The respiratory muscles were unaffected.

Lumbar puncture revealed no pleocytosis with raised protein level of 65mg/dL. Nerve conduction velocities were grossly delayed with slowing of the distal latencies. The culture of the spinal fluid was sterile. The stool samples for the poliovirus were negative. The study for viral markers done during the acute phase of illness showed markedly elevated titres of IgM against the dengue virus. The child made a complete recovery in four weeks being treated with intravenous gammaglobulin.

Discussion

The neurologic symptoms associated with dengue fever are many and have been recognized for more than a century. Classic signs with acute infection are headache, dizziness, delirium, sleeplessness, restlessness, mental irritability and depression. A minority manifest as encephalopathy. Post infectious sequelae are mainly amnesia, dementia, manic psychosis, Reye's syndrome and meningoencephalitis(1-6). However majority of the reports do not describe demyelination as a specific complication.

Simultaneous to the occurrence of the reported cases of Guillain Barre syndrome there was an epidemic of dengue fever in the district of Trivandrum. It had its onset in the month of October 2002. This epidemic was the first of its kind to be reported in Kerala. Guillain-Barre syndrome following dengue fever is not a classically described entity and to our knowledge has not been reported in children. Search for related articles revealed two previous reports. The first was from French Guiana(7) and the second from the West Indies(8). Both the cases occurred in adults.

As in the reported cases in adults, the close temporal association of Guillain-Barre syndrome with occurrence of Dengue fever (serologically proven) indicates that the virus could be the agent that initiated this immunological event that lead to the illness. However, temporal association may not always mean causal relationship.

The nerve injury in Guillain-Barre syndrome is mediated by immunological mechanisms, but the role of the patient's cell-mediated and humoral responses in causing the demyelination has not been fully defined. A role of humoral immunity in the diseases is suggested by findings that sera from GBS patients cause demyelination in appropriate test systems and that plasmapheresis and intravenous administration of immunoglobulin are effective therapies in many of these patients.

Dengue hemorrhagic fever and dengue shock syndrome arise via immunopathologic mechanisms following sequential infection of an individual with these heterologous, antigenically-related serotypes. "Immune enhancement" is thought to play a major role in pathogenesis. Several antigenic determinants for infection-enhancing anti-bodies have been found on the envelope glycoprotein. Thus, it has been postulated that cross-reacting antibodies from a previous dengue infection initiate the cascade that leads to the illness(9).

Thus both the cellular and humoral components of immunity play a crucial role in the immunopathogenesis of both the dengue illness and Guillain-Barre syndrome. The most important factor postulated to initiate the cascade of events leading to very severe dengue illness is the cross-reacting antibodies. The same antibodies could act against the

antigenic determinants on myelin leading on to demyelination.

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