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Neurological manifestations of dengue: A cross sectional study

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Summary *Background:* Dengue is an infectious disease caused by a virus of the flaviviridae family. It is a multi systemic illness causing considerable morbidity and mortality. A spectrum of neurological manifestations has been associated with dengue.
Methods: This was a descriptive cross sectional study including patients diagnosed with Dengue fever (DF), Dengue with warning signs and severe dengue with neurological sequale presenting to the Institute of Neurology, National Hospital of Sri Lanka from June 2011 to August 2012. All patients underwent serology testing for Dengue IgM in blood and CSF as confirmation of the diagnosis.
Results: Seven patients were included. 1/7 had bilateral optic neuritis (ON), 3/7 had a cerebellar syndrome (CS), 2/7 had transverse myelitis (TM) and 1/7 had cranial nerve palsy.

The patient with ON had a post-infectious pattern and protracted recovery.

All patients with CS had bilateral involvement. All had a self limiting course with complete recovery. Two were associated with acute infection.

Both patients with TM had longitudinally extensive disease with one patient experiencing complete recovery. The patient with cranial nerve involvement had isolated 6th nerve palsy.
Conclusions: Neurological manifestations of dengue are diverse. It is important to consider dengue as a cause for the above neurological presentations in hyper endemic territories for the disease.

Introduction

Dengue is an infectious disease caused by a flavivirus. Dengue is recognized as a significant health burden in Asia with considerable morbidity and mortality. With increasing

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travel to the region it is imperative to attain a better understanding of the disease including its rare manifestations.

Sri Lanka is hyper endemic for the disease with 28,473 cases being reported [1] in 2011. A spectrum of neurological manifestations has been associated with dengue and recent studies report an increasing incidence of these neurological sequale [2]. This study describes the neurological sequale of dengue in Sri Lankan patients and relates it to findings in the region and to those in other hyper endemic territories.

Method

This was a descriptive cross sectional study among patients admitted to the Institute of Neurology at the National Hospital of Sri Lanka in Colombo. This is the largest tertiary care neurology referral center in Sri Lanka. This study included serologically confirmed cases of dengue with neurological sequale admitted to the above unit from June 2011 to August 2012. The diagnosis and classification of patients was performed based on the revised WHO classification of 2009 as dengue, dengue with warning signs and severe dengue [3]. Only patients >16 years of age were included.

These patients were diagnosed as having dengue concurrently or within a 2-week period. All patients underwent testing for Dengue IgM in blood and CSF. Patients were evaluated clinically and with investigations including: full blood count, liver function tests, renal function tests, serum electrolytes, coagulation profile. Regional imaging with MRI was performed in all patients. Viral antibodies in blood and CSF (i.e.: Varicella zoster, Epstein Barr, measles, mumps, rubella, herpes simplex, HIV, Japanese encephalitis and Coxsackie viruses), autoimmune screening (ESR, antinuclear antibody) and visual evoked potentials (VEP) were performed based on clinical presentation. All patients underwent fluid management based on current local and WHO guidelines. Other specific management is mentioned with the cases.

Results

Seven patients fulfilling entry criteria were included in the study. All patients were serologically confirmed cases of dengue.

The patient and disease related characteristics are tabulated (Table 1). As demonstrated 6/7 patients were male. One case had a diagnosis of dengue fever while 5/7 had a diagnosis of dengue with warning signs. One had severe dengue with evidence of shock. Cases of severe dengue with hepatic, cardiac or multiorgan involvement were not encountered. Four patients developed neurological sequale during the acute illness while the remainder developed them post-infection.

Optic neuritis (ON)

A 21-year-old male presented with bilateral loss of vision with ocular pain worsened with eye movements. There was no perception of light bilaterally. The patient had dengue fever with warning signs 10 days prior to his visual symptoms. No episodes of hypotension or compensated shock were documented during this episode. He did not demonstrate clinical evidence of autoimmune disease and the autoimmune profile including antinuclear antibodies (ANA) were unremarkable. There was not history of prior exposure to drugs, toxins or alcohol. The patient did not demonstrate evidence of nutritional deficiencies.

The patient had dilated slightly reactive pupils and normal ophthalmoscopy. The rest of neurological examination was normal. VEP was un-recordable bilaterally. A diagnosis of retrobulbar neuritis was made. MRI brain and spine was normal excluding demyelination and space occupying lesions. Lumbar puncture was unremarkable. Intravenous methyl-prednisolone was given for 3 days followed by oral prednisolone for 11 days. The patient had 6/18 visual acuity (VA) bilaterally after one year. The patient did not develop recurrences or other neurological manifestations such as transverse myelitis within the study period.

Cerebellar syndrome (CS)

Three patients demonstrated evidence of bilateral cerebellar dysfunction. They presented with dysarrthria and ataxia and were found to have bilateral nystagmus and dysmetria on clinical examination. Alternate causes of cerebellar syndrome were excluded by means of serology for Varicella zoster, Epstein Barr, measles, mumps, rubella, herpes simplex, HIV, Japanese encephalitis and Coxsackie viruses in blood and CSF. Autoimmune screen was negative.

The onset of CS in the 3 cases ranged from 2 days to 2 weeks from onset of illness (Table 2). All cases showed a self limiting, resolving pattern. The CSF in all cases was unremarkable. MRI showed T2 hyper-intense lesions in the cerebellum in only case 3. The MRI in other patients was normal.

Table 1 Description of patient characteristics and neurological presentations.

Patient	Presentation	Age	Gender	Diagnosis	Timing
1	ON	21	M	Dengue with warning signs	Post
2	Cerebellar	40	F	Severe dengue with shock	Acute
3	Cerebellar	28	M	Dengue with warning signs	Post
4	Cerebellar	25	M	Dengue with warning signs	Acute
5	TM	39	M	Dengue with warning signs	Post
6	TM	31	M	Dengue fever	Acute
7	CN	65	M	Dengue with warning signs	Acute