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Central Nervous System Manifestations and its Outcome in Dengue Fever

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Abstract: ***Dengue is a major public health problem in East Godavari and surrounding districts in the state of Andhrapradesh in South India. Over the last few years, we have been observing varied clinical manifestations of dengue, which rather does not fulfill WHO criteria for making a diagnosis of severe dengue infections like DHF and DSS. A wide range of neurological manifestations were observed in our study. Altered sensorium, seizures, papilloedema, cranial nerve palsy, meningeal signs are among the common manifestations. Encephalitis is an important presentation in hospitalized children. Detection of dengue specific IgM in CSF using ELISA has high specificity and it is difficult to explain the presence of IgM antibody in the CSF other than by viral invasion across the blood brain barrier. In our study IgM in CSF was isolated in 17(35%) of cases, along with mean CSF protein of 84 mg/dl and with CSF mean cell count of 61cells/cmm3 which suggest viral invasion into the CNS. In endemic area dengue encephalitis should be considered in patients who present with the clinical features of encephalitis, whether or not classical manifestation of dengue is present. Standard case definition for dengue encephalitis, if adopted by WHO would help clarify the importance of dengue neurotropism world-wide.***

Keywords: Dengue, Fever, CNS

1. Introduction

Dengue is most rapidly spreading mosquito borne viral disease in the world. In the last 50 yrs, incidence has been increased 30 fold with increasing geographic expansion to new countries and, in the present decade, from urban to rural setting.

An estimated 50-100 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries.

In its most severe form, it manifests itself clinically as dengue hemorrhagic fever and dengue shock syndrome. Recent observations indicate that clinical profile of dengue is changing, neurological manifestations are reported frequently.

The exact incidence of various neurological complications is uncertain. The reported incidence of encephalopathy and encephalitis, the most common neurological manifestations of dengue, have been found to vary between 0.5 -6.2%.

From the pathogenesis point of view, neurological manifestations of dengue can be grouped into three categories:

1) Related to neurotropic effect of virus (encephalitis)
2) Related to systemic complication of dengue infection (encephalopathy)
3) Post infectious like acute disseminated encephalomyelitis, myelitis, Guillain Barre Syndrome, optic neuritis.

Using more sensitive techniques, it has been possible to demonstrate the invasion in the CNS by the virus. The detection of dengue specific IgM antibodies and isolation of dengue virus from CSF of patients with neurologic manifestations ' indicate the neurovirulence of dengue virus and their capability of causing encephalitis.

However the gold standard for diagnosis of dengue encephalitis is isolation of virus in CSF/CNS Since our hospital (GSL Medical College) are tertiary care hospitals, we do see a lot of children with dengue infection including those with neurological manifestations. So an attempt has been made to know the neurological spectrum of dengue virus infection in children and to estimate the IgM levels in CSF of children with neurological complications

Aim and Objectives:

- To assess the incidence, range of neurological manifestations and immediate outcome of dengue viral infection in children with central nervous system manifestations.
- To show the possible neurotropic effect of dengue virus

Methodology Source of Data:
The present study was conducted at GSL Medical College. There has been increasing incidence of dengue fever in this part and also there have been increasing incidence of CNS manifestations. Hence the following study was conducted to find out the incidence of CNS manifestation in children with dengue, spectrum of neurological manifestations and presence of dengue specific IgM antibodies in the CSF.

Method of Collection of Data
All the patients who are admitted in the CG hospitals and BCHI, who showed signs and symptoms of dengue fever and also had positive IgM levels in the blood were included in this study.

Sample of size- 100 children

Inclusion criteria: All children with dengue fever-seropositive for IgM antibodies.

Exclusion criteria: Children with fever but negative for dengue serology.

Study design: It is a prospective study of all serum positive

dengue patient admitted to the hospital

Investigations:

- CBC
- Serum IgM / IgG for dengue antibodies
- LFT
- PT / APTT
- Chest X-ray
- LP – CSF analysis-Cell type / cell count,-Protein / chloride / sugar
- IgM for DENGUE ANTIBODIES
- CT scan

Case Definition for dengue encephalitis:

1) Fever
2) Reduced consciousness-Not explained by
   - Acute liver failure
   - Shock
   - Electrolyte disturbance
   - Intracranial hemorrhage
   - With corroborating laboratory findings
   - Dengue virus or IgM in serum or CSF
   - Neuroimaging suggestive of viral encephalitis

Abbreviations

CNS: Central Nervous System
CSF: Cerebrospinal fluid
DF: Dengue Fever
DHF: Dengue Heamorraghic Fever
DSS: Dengue Shock Syndrome

2. Results

Table 1: Incidence of Neurological Manifestations

	Dengue fever	F with CNS involvement
No. of cases	100	40

Table 2: Age distribution

Age	DF with CNS manifestations	DF without CNS
<1 yr	1	2
1-6 yrs	17	22
>6 yrs	22	36

Out of 100 cases of dengue fever, 40 children who had neurological involvement, mean age of presentation was 6.9 yrs. The youngest was 6 month old infant and eldest was 16 yrs old male. In the other group mean age of presentation was 7.18, the youngest was 6 month infant and eldest was 15 yrs

Table 3: Gender distribution

Gender	DF with CNS involvement	DF without CNS
Male	23	35
Female	17	25

Table 4: Clinical Spectrum of Cases

Clinical spectrum of cases	Total no of cases (N=100)	No of cases in DF with CNS
DF	42	7
DHF	32	13
DSS	26	10

Out of total 100 cases studied, 42 children met WHO specified criteria for DF, 32 DHF and DSS respectively with dengue fever, 32 children had DHF and 26 patient had DSS. Clinical spectrum of cases in with neurological involvement (40cases) was dengue fever 17 cases, DHF in 13 cases and DSS in 10 cases.

Table 5: Sign and Symptoms in Patients without Neurological Manifestations

Symptoms	Cases (n=60)	Percentage
Fever	60	100%
Headache	18	30%
Vomiting	30	50%
Abdominalpain	15	25%
Arthralgia	12	20%
Malena	6	10%
Lymphadenopathy	33	55%
Rash	17	28.3%
Puffinessofeye	18	30%
Petechiae	18	30
Hepatomegaly	47	78.3%
Spleenomegaly	23	38.3%

In our study, the most common symptom was fever (100%) followed by vomiting (50%), headache (30%), abdominal pain (25%), arthralgia (20%), malena (10%). The most common signs were hepatomegaly (78.3%), followed by Lymphadenopathy (55%), splenomegaly (38.3%), petechiae and puffiness of eye (30%) and rash (28.3%).

3. Discussion

Dengue infections is one of the most important arboviral infections of humans and is one of the most important tropical infectious disease in the world.

The occurrence of neurological manifestations in dengue infection has been recognized for long. In previous reports of neurologic involvement in dengue infections, the observed “encephalopathy” was thought to be due to prolong shock, along with fluid extravasation, cerebral edema, hyponatremia and liver failure

Recently however, direct neurotropic potential of the virus has been recognized In India too; neurological complications of dengue have been reported.

In the present study all the 100 cases studied were serum IgM positive for dengue infection. Out of these 100 cases, 40 children had symptoms and signs pertaining to CNS involvement. Hence the incidence of neurological involvement in our study was 40%, which we believe is very high as compared to other studies.

The median age of presentation of children in our study is 6.9 yrs (0.6-16 yrs). Similar observations were made by others. The following table shows age distribution observed in various other studies.

The incidence of male children that were affected is slightly more in our study, the ratio being 1.7:1.

Incidence of neurological involvement was more in the children who met the clinical features of WHO specified criteria of only dengue fever. Similar observation was made

by Misra et al which suggest that neurological involvement may not be necessarily due to shock or bleeding. It may be due to direct neurotropic effect of the virus.

In present study fever (100%) is a predominant symptom followed by altered sensorium (82.5%), seizure (77.5%), vomiting (57.5%) and headache (52.5%). In present study, however altered sensorium and convulsion were the most frequent presentation.

An interesting observation that we made in our cases were that the presence of papilloedema and meningeal sign which were significantly more being 32.5% and 80% respectively.

The mean raise of transaminase in our study were slightly higher CSF pleocytosis is an indication of the inflammation of meninges and encephalon probably due to direct viral invasion. In our study CSF pleocytosis was seen in 82% of the cases.

Though the gold standard of diagnosing viral encephalitis is isolation of virus either from neural tissue or CSF, however detection of viral specific IgM in the CSF is considered as an indication of viral replication in the CNS. In the present study CSF IgM was positive in 35% of the cases, which is little less when compared to the other studies.

The reason for low percentage of positivity of IgM in CSF in our study, could be, because of we used CSF in 1:10 dilution as per the guidelines given by NIV Pune, the manufacturer of the kit. In one study, done by Soares et al CSF 1:2 dilution was used, probably we could have got more positive test results if lesser dilution was used.

4. Conclusion

Dengue is a major public health problem in East Godavari and surrounding districts in the state of Andhrapradesh in South India.

Over the last few years, we have been observing varied clinical manifestations of dengue, which rather does not fulfill WHO criteria for making a diagnosis of severe dengue infections like DHF and DSS. A wide range of neurological manifestations were observed in our study. Altered sensorium, seizures, papilloedema, cranial nerve palsy, meningeal signs are among the common manifestations.

Encephalitis is an important presentation in hospitalized children. Detection of dengue specific IgM in CSF using ELISA has high specificity and it is difficult to explain the presence of IgM antibody in the CSF other than by viral invasion across the blood brain barrier.

In our study IgM in CSF was isolated in 17(35%) of cases, along with mean CSF protein of 84 mg/dl and with CSF mean cell count of 61cells/cmm3 which suggest viral invasion into the CNS.

In endemic area dengue encephalitis should be considered in patients who present with the clinical features of encephalitis, whether or not classical manifestation of dengue is present.

Standard case definition for dengue encephalitis, if adopted by WHO would help clarify the importance of dengue neurotropism world-wide.

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