

# Unusual neurological manifestation of dengue fever

**ABSTRACT: Background** -Neurological manifestations are considered to be a rare part of dengue fever. The frequency of neurological involvement is not exactly known. Only few cases have been reported in literature from South Asia and Africa. Dengue fever is an arboviral infection with systemic involvement. Neurological complications can occur in the form of encephalitis, seizures, encephalopathy, aseptic meningitis, intracranial haemorrhage, polyneuropathies and Guillain barre syndrome, transverse myelitis etc. These features can be associated with other comorbidities and complications like prolonged shock.

**Case presentation-** We are present a case of 50 years female resident of Punjab India, who presented to us with fever of 4 days duration, myalgias, altered mental status, followed by sudden onset paraparesis with urinary incontinence. On examination, there was flaccid paraparesis, areflexia with patchy area of sensory loss without any definite level, neck rigidity and no other significant finding. Routine investigations showed thrombocytopenia, with normal liver and renal functions, tropical fever serology was positive for dengue IgM. After recovery of thrombocytopenia, cerebrospinal fluid examination was done which showed 40 cells predominantly lymphocytes, high protein and normal sugars, fluid was also positive for dengue IgM and dengue PCR. Nerve conduction studies showed acute sensory motor axonal neuropathy. Thus, finally a diagnosis of dengue encephalitis with Guillain barre syndrome was made and patient was started on Immunoglobulin therapy. Patient did respond to the treatment and has now recovered completely over 3 months.

**Conclusion-** Neurological complications which occurs after dengue infection due to physiological response of body to dengue virus, can affect body in different forms and systems. Usually the central nervous system involvement and peripheral nervous system involvement and local complication due to direct viral effect like myositis and periodic paralysis occur at different time, but rarely both CNS (encephalitis) and PNS (GBS) complication can occur in same patient at the same time.

**INTRODUCTION:** Dengue fever is a common arboviral infection, but its neurological features are equally uncommon. The incidence rate of neurological manifestation in dengue fever has increased from 0.5 to 20% in recent years.<sup>1</sup> Neurological manifestations have been reported in individuals of all age groups.<sup>2</sup> Dengue fever has variable clinical manifestation

ranging from asymptomatic to severe haemorrhagic fever. High body temperature, high haematocrit, thrombocytopenia, rashes and transaminitis are independent risk factors for neurological complications.<sup>3</sup> Neurotropic feature of dengue virus was detected by Miagostovich et al. by assessment of viral proteins, ribonucleic acid, and immunoglobulins in cerebrospinal fluid.<sup>4</sup> There are four serotype of dengue virus (DENV-1, DENV-2, DENV-3, DENV-4). Among them DENV-2 and DENV-3 are most commonly related to neurological complications. On the basis of pathogenesis, neurological complications can be divided into three groups: Group-A due to neurotropic nature of virus like meningoencephalitis and myelitis, Group-B due to direct effect of active viral infection like ischemic and haemorrhagic stroke, encephalopathy, posterior reversible encephalopathy syndrome, papilledema, myositis, and hypokalemic paralysis and Group-C post infectious neurological complications like Guillain-Barre Syndrome, Miller-Fisher syndrome, vasculitis, neuro ophthalmological disorder (neuromyelitis optica, optic neuritis, maculopathy) and neuritis (oculomotor palsy, abducens nerve palsy, facial nerve palsy, brachial neuritis, phrenic nerve palsy, long thoracic nerve palsy).<sup>5</sup>

Despite diverse range of post infectious neurological complications of dengue infection, coexisting manifestation of one category with other has not been reported very much in the literature till now. We are presenting a Dengue IgM serology positive case of dengue fever with meningoencephalitis and acute sensory motor axonal neuropathy.

**Case Presentation:-** A 50 years female presented to us with history of fever of 5 days duration with headache and myalgia followed by sudden onset bilateral lower limb weakness and altered mental status with urinary incontinence, on general physical examination she was having mild pallor with no other significant finding on systemic examination she was having neck rigidity, flaccidity of both lower limb with patchy area of sensory losses, with absent deep tendon reflexes, with urinary incontinence without any clinical evidence of optic neuritis and other cranial nerve involvement. Patient was evaluated outside our hospital by primary investigation in which she was having thrombocytopenia, anaemia, with normal leucocyte counts, liver function shows transaminitis with normal bilirubin, renal function was normal, in view of thrombocytopenia tropical fever work up was done which was found to be positive for dengue IGM,

After recovery of thrombocytopenia, in view of altered mental status patient was subjected for cerebrospinal fluid examination, which showed 40 cells out of them 60 percent were lymphocytes, 40 percent were neutrophils, high protein (108 mg%) and normal sugars 54 (mg%), with normal adenosine deaminase levels, due to positive dengue serology cerebrospinal fluid was sent for dengue IGM and dengue PCR, both found to be positive while all other viral (HSV, JEV, CMV, EBV) CSF serologies and nucleic acid amplification studies were negative, in view of paraparesis patient was subjected for imaging and neurophysiological studies in which magnetic resonance imaging of brain on T2 weighted images showed altered area of signal intensity in bilateral parasagittal and precentral gyrus (Figure -1) and T1 weighted images showed hyperintensity in parasagittal region, and bilateral hippocampus left peritrigonal region and bilateral cerebral peduncle without any evidence of demyelination, and spine was found to be normal, nerve conduction studies was suggestive of acute sensory motor axonal neuropathy. Hence diagnosis of dengue fever with meningoencephalitis and Guillain barre syndrome was made patient was started on human immunoglobulins with completion of therapy for 5 days patients become conscious

weakness of lower limb was start improving, in period of 25 days she was recovered completely.

**DISCUSSION:-** Encephalitis is considered as most severe manifestation of dengue fever, diagnosis is usually criteria based proposed by Soares and Marzia<sup>6</sup>. According to them normal CSF cellularity not rule out dengue encephalitis, even normal CSF cells with viral meningitis and encephalitis, dengue is considered as first possibility in dengue endemic region, second possibility is herpes simplex virus while in our case CSF was lymphocytic predominant but it was also positive for dengue IGM and PCR. Baldcara et al.<sup>7</sup> and Madi et al.<sup>8</sup> reported that magnetic resonance imaging may be normal or non specific finding in case of dengue encephalitis, while in our case hyperintense signal area in bilateral thalami on FLAIR sequence was present with blooming in central part of thalami on SWI sequence. Palma-da Cunha-Matta A et al.<sup>9</sup> reported two case of immune mediated CNS involvement following dengue infection one was post infectious acute disseminated encephalomyelitis and other was Guillain Barre syndrome, Magnetic resonance imaging of ADEM (acute disseminated encephalomyelitis) patient showed T2 hyperintensity in cerebral peduncle, lentiform nuclei and internal capsule on both side of brain and CSF examination of GBS patients showed albumin cytological dissociation and NCV showed polyradiculoneuropathy, while in our case only bilateral thalami was affected with overlapping of same CSF features in single patient, although total 20 case report has been documented in the literature where patient had various neurological complication following dengue fever but coexisting two neurological complication of different category has not been reported till now our case report probably the first case with two different neurological complication of different category in a single patient following a classical dengue infection.

**CONCLUSION :-** Neurological complications which occurs after dengue infection due to physiological response of body to dengue virus, can affect body in different forms and system usually central nervous system involvement and peripheral nervous system involvement and local complication due to direct viral effect like myositis and periodic paralysis occur at different time, but in our case study both CNS (encephalitis) and PNS (GBS) complication seen in a single patient after a single episode of dengue fever which is rare, further studies in this field to know exact frequency of coexisting neurological complication in dengue patient need to be recommended, because morbidity and mortality association are high with such kind of presentation.

### **Abbreviations**

**CNS-**Central nervous system

**PNS-** Peripheral nervous system

**HSV-**Herpes simplex virus

**JEV-**Japanese encephalitis virus

**CMV-**Cytomegalovirus

**EBV-** Epstein barr virus

**GBS-** Guillain Barre syndrome

**DENV-**Dengue virus

**ADEM-**Acute disseminated encephalomyelitis

**PCR-** Polymerase chain reaction

**Availability of data and materials-**The data used and/or analyzed during the present study are available from the corresponding author on reasonable request.

**Declaration-**We wish to confirm that there are no conflicts of interest associated with this publications and there has been no significant financial support for this work that could have influenced its outcome

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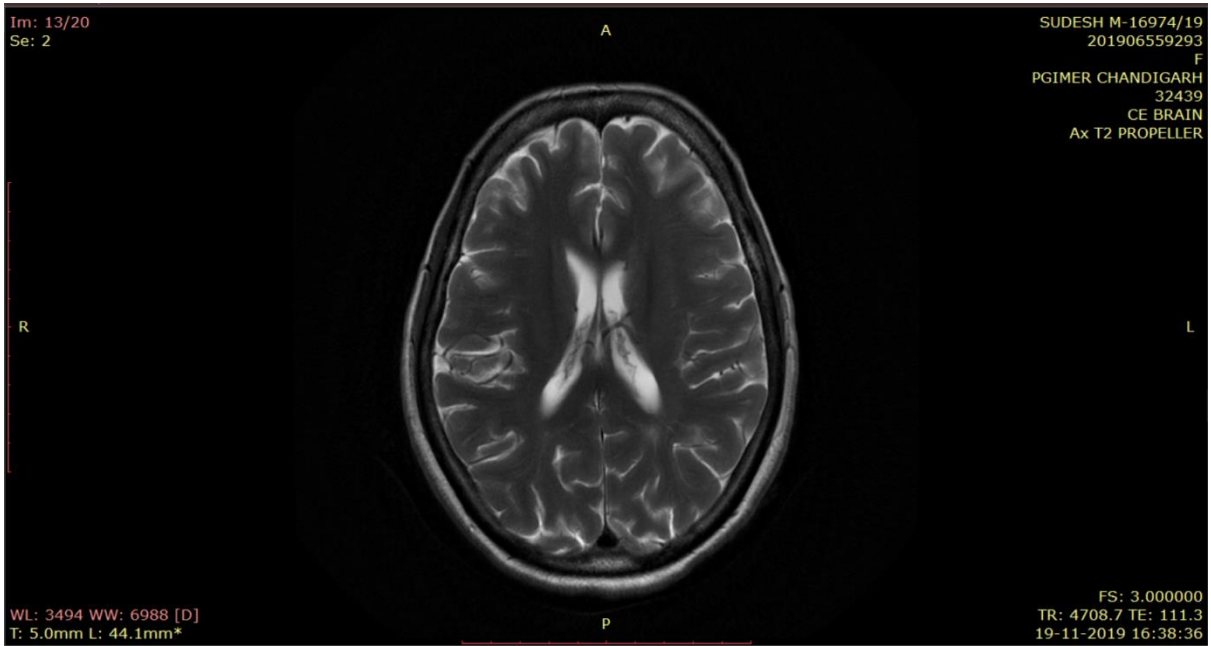


FIGURE 1. T2 WEIGHTED IMAGE OF MR SHOWED ALTERED AREA OF SIGNAL INTENSITY IN BILATERAL PARASAGITTAL AND PREANTRAL GYRUS

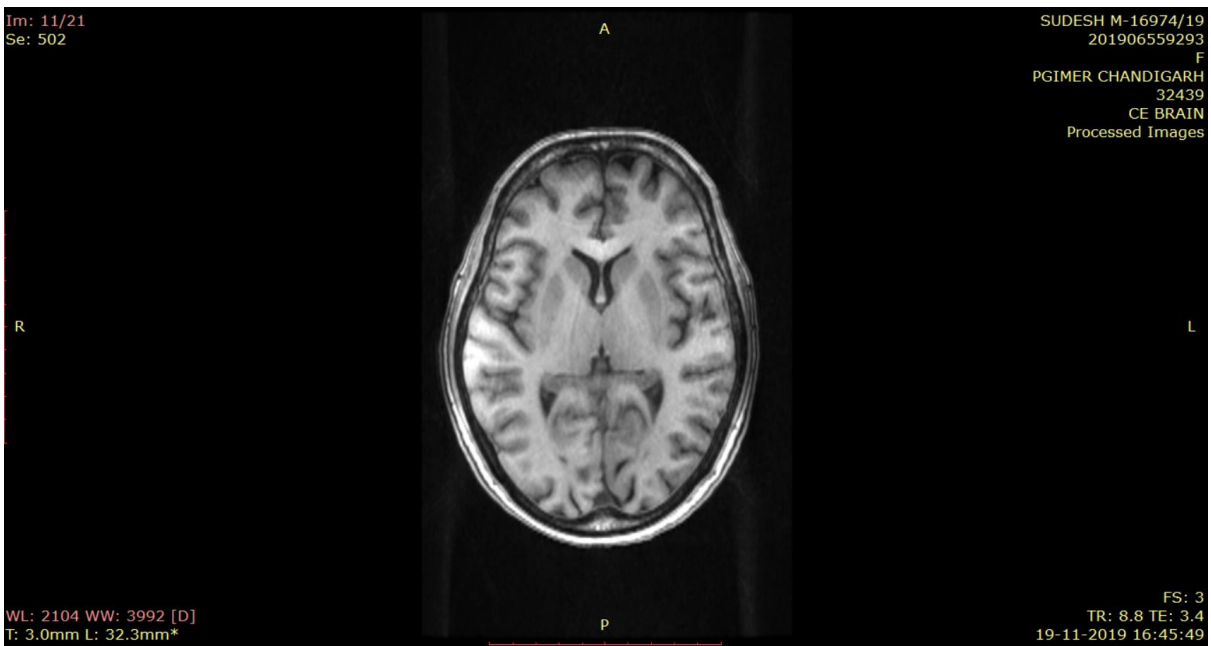


FIGURE 2 T1 WEIGHTED IMAGE SHOWED HYPERINTENSITY IN PARASAGITTAL REGION AND BILATERAL HIPPOCAMPUS LEFT PERITRIGONAL REGION AND BILATERAL CREBRAL PDUNCLE