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# NEUROLOGICAL MANIFESTATIONS AS PRESENTING FEATURE IN DENGUE FEVER

Shahid Ahmed, Nadir Ali\* and Waheed Uz Zaman Tariq\*\*

## ABSTRACT

Dengue fever (DF), caused by dengue viruses, presents classic dengue fever, dengue hemorrhagic fever, and dengue shock syndrome. A young man presented with 5 days history of fever, body aches, headache, vomiting and one day history of drowsiness and a generalized tonic clonic fit. He was afebrile and hypotensive with platelets count of  $24 \times 10^9/l$ , and serum IgM DENV positive. Computerized tomography scan of the brain revealed intracerebral haemorrhages in both cerebral hemispheres. He was managed with supportive care and 20% mannitol infusion, his headache and drowsiness rapidly improved. Platelet count rose to  $60 \times 10^9/l$  on 2nd day and  $199 \times 10^9/l$  on 7th day of admission. He remained afebrile during hospital stay and was discharged from hospital on 8th day of admission, when he was almost asymptomatic.

**KEY WORDS:** *Dengue hemorrhagic fever. Intracranial bleeding. Thrombocytopenia. Neurological features.*

## INTRODUCTION

Dengue fever (DF) is caused by dengue viruses (DENVs), members of the Flaviviridae family. DENVs contain four closely related serotypes: DENV-1, DENV-2, DENV-3 and DENV-4.<sup>1</sup> Clinically, three groups are recognized. Classic dengue fever (DF) is characterized by acute febrile illness, headache, retro-orbital pain, nausea, vomiting, and myalgias. Dengue hemorrhagic fever (DHF) is characterised by symptoms of DF along with hemorrhagic manifestations, and dengue shock syndrome (DSS) is characterised by capillary leak and shock. The majority suffers from uncomplicated dengue fever but about 3% of the patients develop potentially fatal disease. The classic dengue fever occurs in non-immune persons while DHF and DSS usually occurs during a second dengue infection with pre-existing immunity to a heterogeneous dengue virus serotype.

Neurological manifestations such as seizures, encephalopathy/encephalitis, have been reported only rarely.<sup>2,3</sup> Some of these cases did not manifest other typical features of dengue infection.

We document below a rare presentation of dengue fever with shock, neurological manifestations and intracranial bleeding without extracranial manifestations of mucosal or skin haemorrhages.

## CASE REPORT

A young man of 23 years of age presented with 5 days history of fever, body aches, headache, vomiting and one day history of drowsiness and a generalized tonic clonic fit. He remained admitted in a local hospital due to fever, headache and

vomiting and was treated with injections Artemether and

Ceftriaxone till the morning of the day he was brought to the CMH, Malir Cantt., Karachi. He had a single brief generalized tonic clonic fit in the morning and remained drowsy complaining of severe headache. There was no history of epistaxis, gum bleeding, haematuria or malaena. On examination, he was a young man of thin built, ill-looking, lethargic and drowsy but communicative and cooperative. He was afebrile with a pulse rate of 96 beats per minute and a blood pressure 80/60 mmHg. There was no rash, purpuric spots or ecchymosis detectable on his body. Neck was supple and Kerning's sign was negative. Ophthalmoscopy revealed normal discs and there were no focal signs in the limbs. He was not pale or jaundiced. There was no lymphadenopathy or hepatosplenomegaly on clinical examination. Respiratory and cardiovascular systems were also normal. His haemoglobin was 13g/dl, TLC  $7.4 \times 10^9/l$  and platelets count was  $24 \times 10^9/l$ , ALT 73 u/l. Alkaline phosphatase was 296 u/l, and bilirubin was 14.4 umol/l. Prothrombin time and partial thromboplastin time were within normal limits. Serum sodium was 142 mmol/l, potassium was 4.2 mmol/l, chloride 101 mmol/l and bicarbonate 22.8 mmol/l, urea 7.5 mmol/l and creatinine 98 umol/l, plasma sugar random was 5.9 mmol/l.

Computerized tomography scan of the brain revealed intracerebral haematomas in both cerebral hemispheres, the largest one in right parietal region,  $2.6 \times 2.2$ cm (Figure 1), with surrounding oedema and minimal mass effect over the right lateral ventricle. Dengue fever was suspected due to ongoing epidemic of dengue fever in the region, and serum sample was collected for IgM dengue virus (IgM DENV).

He was treated with 20% mannitol infusion and supportive care; his headache and drowsiness rapidly improved. Platelet count rose to  $60 \times 10^9/l$  on 2nd day and  $199 \times 10^9/l$  on 7th day of admission. He remained afebrile during hospital stay and was discharged from hospital on 8th day of admission, when he was almost asymptomatic. Serum IgM DENV was positive.

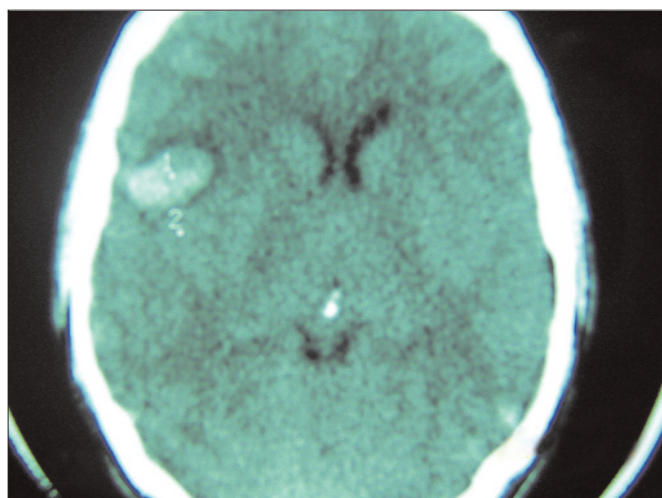
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**Figure 1:** Large haematoma in right parietal region, 2.6 x 2.2 cm.

He remained symptom-free and his platelet counts were followed fortnightly for two months in outdoor clinic, which remained within normal limits along with rest of the blood counts.

## DISCUSSION

Dengue haemorrhagic fever is primarily a disease of children under 15 years in hyperendemic areas. The disease is characterised by increased capillary permeability and haemostatic changes. If major plasma leakage occurs, it usually develops near defervescence. Patients may develop effusions and ascites with a variable amount of bleeding. Mortality can be as high as 10-20% without early appropriate treatment, but it is as low as 0.2% in hospitals with staff experienced in managing the disease. Warning signs that dengue shock syndrome is impending include sustained abdominal pain, persistent vomiting, change in level of consciousness (irritability or somnolence), a sudden change from fever to hypothermia, and a sudden decrease in platelet count. Rare presentations of infection include severe haemorrhage, jaundice, parotitis, and cardiomyopathy. Unusual neurological presentations include mononeuropathies, polyneuropathies, encephalitis, and transverse myelitis. Encephalopathy occurs occasionally and may result from cerebral oedema, cerebral haemorrhage, liver failure, or electrolyte imbalances.<sup>4</sup>

In this case DHF with DSS was suspected and neurological presentation were due to unexplained thrombocytopenia associated with fever. The differential include Crimean-Congo hemorrhagic fever, dengue fever, malaria, and typhoid fever.<sup>5,6</sup> Although usual haematological presentation of DF is bicytopenia but isolated thrombocytopenia has been reported in a considerable number of cases.<sup>7</sup> The other reason for suspecting dengue aetiology was the past and ongoing epidemics of DF in Pakistan.<sup>7,8</sup> Detection of IgM DENV in serum samples is highly suggestive of DHF.<sup>9</sup> The treatment of DHS is generally supportive, and no specific antiviral drug

therapy is required. We treated the patient on similar lines. Dengue fever is endemic in Pakistan and probably has been underreported. Most of the cases reported worldwide and in Pakistan are of either classic DF or DHF. Presentation as DSS is rare, and DSS along with neurological manifestations and intracranial bleeding without extracranial hemorrhagic manifestations is even rarer. The epidemics of dengue fever from almost all parts of the country have been reported since 1994.<sup>7</sup> Second infection by heterotype virus may lead to DHF or DSS, cases with second infection and more serious manifestation of disease are expected.

The actual number of human infections is probably much higher than the number reported. DF is usually non-specific febrile illness that resolves with supportive therapy and can be confused easily with common cold, malaria, typhoid or sore throat but it renders the community susceptible to more serious infection by other serotypes, and more serious outcome. DF is an emerging global health problem, the disease is notorious in its capability to spread and is difficult to eradicate due to poor control on mosquito eradication in tropical and subtropical countries. In 1970, only nine countries had known epidemics of DHF, but this number has increased manifold. According to World Health Organization, about 50 million cases of dengue occur worldwide annually. During epidemic, rate of infection among the susceptible is often between 40-50% but may reach to 80-90%. Failure to identify DHF as emerging health problem may lead to more serious outbreaks.

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