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Dengue Encephalitis and Encephalopathy are Different Entity - Case Study

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Abstract: ***Dengue encephalitis is a different entity, which possibly occurs due to direct neuronal infiltration by the dengue virus. Encephalopathy is a rare though well-known neurological complication of dengue infection. These two different cases, therefore, highlight the lack of a definite scientific explanation of the exact pathogenesis behind neurological syndromes in dengue infection with minimum clinical signs. A 23-year-old female patient (Case 1) was admitted with a history of fever, headache and joints pain for the 4 days, followed by two episodes of seizures on the fourth day of illness and subsequently developed altered sensorium. Her both dengue IgM and IgG dengue antibodies were positive. Her lumbar puncture revealed that evidence of lymphocytic pleocytosis with normal protein and sugar. She has been diagnosed with encephalitis. A 31-year-old gentleman (Case 2) was admitted with the history of fever, myalgia, arthralgia, and headache for five days duration. His blood test confirmed that both IgM and IgG antibodies were positive. In Cerebrospinal fluid(CSF) analysis revealed that protein and sugar were normal and no evidence of pleocytosis. He was diagnosed with dengue fever complicated with encephalopathy. The pathophysiology of dengue encephalitis and encephalopathy are a benign but potentially fatal disease. However, encephalitis must always be distinguished from an encephalopathy, which may present similar manner. It is vital for developing a more effective management plan.***

Keywords: Dengue encephalitis, and dengue encephalopathy

1. Introduction

The dengue virus fits into the Flaviviridae family. There are four closely related, but antigenically different virus serotypes: DENV1 to DENV4[1]. The infection delivers life-long protective immunity to the same subtype, but no immunity against the other three serotypes. Furthermore, the previous infection with a different subtype increases the chances of developing dengue hemorrhagic fever [2]. The clinical spectrum of dengue fever ranges from asymptomatic infection, dengue fever(DF), dengue hemorrhagic fever(DHF) and dengue shock syndrome(DSS). However, there are many rare presentations were reported throughout the world. The neurological symptoms are wide-ranging and related to types of infection and immunity of the cost. A headache, alteration of consciousness, irritability, insomnia, seizures and focal neurological deficit associated with encephalitis, encephalopathy, intracerebral haemorrhage and stroke pictures are the most common symptoms observed during the acute dengue. The incidence of intracerebral haemorrhage with dengue shock can be a fatal [3]. Even after dengue fever or during the post-dengue stage, some patients were developed polyradiculoneuritis, encephalomyelitis, neuromyelitis optica, polyneuropathy, and mononeuropathy. At present, neurological manifestations related to dengue infections are increasingly been observed and appears as a challenge for medical practice.

Acute viral encephalitis founds as a medical emergency. Encephalitis is the most common neurological manifestation of dengue infection. In most of the time, the presence of focal neurological signs and focal seizures will distinguish encephalitis from encephalopathy. Herpes simplex encephalitis [4], varicella zoster virus, Epstein-Barr virus, mumps, measles, influenza [5], and enteroviruses are the commonest sporadic acute viral encephalitis in the world [6]. In case of encephalitis, a degree of meningeal involvement is always present, and the clinical symptoms reflect both diffuse and focal cerebral pathology as well as meningitis]7]. The grade of altered consciousness is a degree of the severity of acute encephalitis and it may range from drowsiness to coma. Seizures, both focal and generalized, are common [8].

However, encephalitis must always be differentiated from an encephalopathy, which may present similarly but consequences from metabolic disturbances caused by liver and renal failure, intoxications, systemic infections, and anoxia, rather than from inflammation. The aim of the study is to differentiate the dengue encephalitis from encephalopathy.

2. Case Presentation

Case 1

A 23-year-old female patient was admitted with a history of fever, headache and joints pain for the 4 days, followed by two episodes of seizures on the fourth day of illness and subsequently developed altered sensorium. On admission, she was febrile (38.1°C), without any signs of respiratory distress, skin rash, icterus, or mucosal bleeds. She was drowsy with a Glasgow Coma Score (GCS) of 7/15 but. without any meningeal signs. The rest of the systemic examination was normal. Urgent blood report and non-contrast computerized tomography of the head(CT-head) was taken it was normal. Unfortunately, her white cells count(WCC) revealed that neutropenia with lymphocytosis and with very low platelets (WCC 3x 10^9/l, platelets 23x10^9/l). Since very low platelets we didn't proceed for lumbar puncture. The fifth day of the fever, a blood test revealed that both IgM and IgG dengue antibodies were positive. At the bedside, she was diagnosed with dengue encephalitis in view of persistent fever with the history of seizures and altered sensorium. However, as her platelets

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count low we didn't do the lumbar puncture, she was started intravenous antibiotics and acyclovir. The seventh day of the fever, her GCS was improved by two. Her platelets started to raise, we did a lumbar puncture, which revealed that evidence of CSF lymphocyte pleocytosis with normal protein and sugar. We excluded HSV and tuberculosis in the CSF. Rest of the investigations were normal. The ninth day of the admission, she improved well and subsequently, we stopped all antibiotics and antiviral treatment. She was diagnosed with dengue encephalitis.

Case 2

A 31-year-old gentleman was admitted with the history of fever, myalgia, arthralgia, and headache for five days duration. His blood test revealed as a viral pattern with thrombocytopenia. His blood test confirmed that both IgM and IgG antibodies were positive. The seventh day of the admission his fever was settled but, he confused and showed bilateral horizontal nystagmus. His liver function test was altered however his renal function was normal. The same day he became drowsy and agitated. His oxygen saturation has fluctuated, subsequently, he was intubated and connected with mechanical ventilation. Urgent non-contrast computerized tomography of the head(CT-head) was taken which was normal subsequently a magnetic resonance imaging (MRI) scan was taken which was normal. WCC was $2.3x10^9$/l, platelets were $55x10^9$/l, ALT was 1050u/l, AST was 780u/l, serum creatinine was 1.1mg/dl, and Leptospira antibody was negative. In Cerebrospinal fluid(CSF) analysis revealed that protein and sugar were normal and no evidence of pleocytosis. Herpes simplex and Japanese encephalitis viral serology were normal in the CSF. The patient was on the ventilator support for a nearly one-month period before recovered fully without any neurological defects. He was diagnosed with dengue fever complicated with encephalopathy.

3. Discussion

One of the atypical manifestations of encephalitis is the most common neurological manifestation of dengue infection and the main symptoms include seizures, altered consciousness, and headaches [9]. A significant proportion of individuals with encephalitis presents the classical symptoms of dengue infection such as myalgias, diarrhea, joint or abdominal pain, rash and mucosal bleedings. However, the diagnostic criteria for dengue encephalitis consist of: fever and acute signs of cerebral involvement associated with the presence of anti-dengue IgM or dengue antigen in the serum and/or CSF added to the exclusion of other causes of viral encephalitis. Interestingly, our patient (Case 1) fulfilled all the criteria.

However, we had a confusion that whether this patient had any involvement of leptomeninges(Meningitis). In case of encephalitis, a degree of meningeal involvement is always present, and the clinical symptoms reflect both diffuse and focal cerebral pathology as well as meningitis [7]. But, clinically she did not show any neck stiffness and subsequent CSF report revealed leucocyte pleocytosis with normal protein and sugar, this clinical and biochemical finding clearly indicated that there is no meningeal involvement. A raised CSF leukocyte count rarely provides the final diagnosis but may indicate an inflammatory process within the central nervous system and is essential in guiding succeeding decision making and management [10]. However, CSF analysis may be normal in 50% of patients with encephalitis [11]. Serology can succeed where both culture and polymerase chain reaction(PCR) fail. However, encephalitis secondary to dengue infection usually has a favorable outcome.

Encephalopathy due to dengue is a recognized complication, however unusual, an entity with incidence fluctuating from 0.5% to 6.2%. However, in some cases, neurological symptoms remain unanswered, however, direct neuronal infiltration by the virus may be the key to pathogenesis [12]. Furthermore, immune-mediated encephalitis usually happens because of a post-infectious course such as acute disseminated encephalomyelitis (ADEM), typically the following infection with measles, mumps, or rubella virus infection [13,14]. The characteristic clinical picture is a younger person with a history of vaccination or infection presenting shortly, without fever at the onset of symptoms. Additionally, multifocal neurological signs affecting both the brain and spinal cord and possibly the peripheral nerve roots [15]. It should also be valued that ADEM can also present with a very restricted neurological picture such as transverse myelitis, optic neuritis, and cerebellar ataxia [16]. A magnetic resonance imaging (MRI) findings in dengue differ, MRI could be normal but hemorrhages, cerebral edema, and focal abnormalities involving the basal ganglia, hippocampus and thalamus can be seen. However, in case of dengue complicated with encephalopathy, there is no obvious structural damage, where MRI was normal. In our patient, MRI was normal [17].

4. Conclusion

Dengue fever (DF) is related with fever, headache, myalgia, joint pain, and rash, though DHF is considered by the symptoms in DF shared with unprompted bleeding and plasma leakage which may progress to dengue shock syndrome(DSS). Dengue encephalitis and encephalopathy are the rare phenomena and their mechanism of pathogenesis has not been understood yet. The foremost symptoms of dengue encephalitis are a headache, seizures and altered consciousness. In contrast to aseptic viral meningitis, neuropsychiatric symptoms frequently prevail in encephalitis, for example, hallucinations, psychosis, personality changes, and agitation. However, encephalitis must always be distinguished from an encephalopathy, which may present similarly but consequences from metabolic disturbances caused by liver and renal failure, intoxications, systemic infections, and anoxia, rather than from inflammation.

5. Abbreviation

DF-dengue fever, DSS- dengue shock syndrome, AEDM-acute disseminated encephalomyelitis, CSF- Cerebrospinal fluid, WCC- white cells count, DHF- dengue hemorrhagic fever

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Ethical Approval and Consent to participate

Ethical approval is not applicable, but written consent for participation was taken from the patients

Consent for publication

Written informed consent was obtained from the patients for publication of this case report

Availability of supporting data

All data was written in the case history

Competing interests

The author declare that they have no competing interests.

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Authors' contributions

Author M.U prepared the initial manuscript, participated in drafting and editing the manuscript, and literature review

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