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Dengue fever associated cerebral hemorrhages, a rare, poorly understood entity in an era of dengue epidemic: A case series and literature review

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Abstract

Dengue is caused by a flavivirus, which may be a vector borne RNA virus with four anti-genically distinct serotypes (DEN 1, DEN 2, DEN 3 and DEN 4). Neurological manifestations are rare compared to other complications of the disease. Encephalopathy, encephalitis, aseptic meningitis, intracranial hemorrhages, thrombosis, mono-neuropathies / polyneuropathies, Guillain-Barre syndrome and myelitis are reported. Neurological manifestation in dengue haemorrhagic fever usually results from multisystem dysfunction secondary to liver failure, cerebral hypoperfusion, electrolyte imbalance, shock, cerebral edema and hemorrhage associated with vascular leak. The occurrence of brain hemorrhage during a case with dengue shock are often serious and results in death. The occurrence of brainstem hemorrhage are often a really serious fatal situation. We report this case series of dengue haemorrhagic fever with multiple intracranial, sub arachnoid hemorrhages and sub-dural hematoma causing brainstem herniation. Case 1: A 25-year-old previously healthy woman was admitted on third day of fever with thrombocytopenia. Critical phase started on 5th day with evidence of pleural effusion and moderate ascites. 31 hours into critical phase, she developed headache, altered level of consciousness, limb rigidity and respiratory depression without definite seizures. Non-contrast CT brain done at tertiary care level revealed diffuse intra cranial hemorrhages and sub arachnoid hemorrhages in right frontal, parietal, occipital lobes and brainstem, cerebral oedema with an acute subdural hematoma in right temporo-parietal region. Her platelet count was 40,000 at this point with signs of vascular leakage. She was intubated and ventilated with supportive care. Later on, she developed features of cranial diabetes and it skilled intranasal desmopressin therapy. In spite of above measures signs of brainstem herniation developed and she or he succumbed to the illness on day 8. Dengue was confirmed serologically. Case 2: A 24 year old previously healthy was admitted on 2nd day of fever with constitutional symptoms and no bleeding manifestations. Clinical, hematological and serological parameters confirmed dengue infection. On 5th day of illness, she entered into leaking phase, but didn't have evidence of any bleeding Intra Cranial Hemorrhage (ICH) in right lobe deep substantia alba area related to perilesional oedema and midline shift. Bleeding into the proper ventricle and little Subdural Hematoma (SDH) were also noted in right lobe area. Her platelet count at the time of development of hemorrhages was 32,000 and International Normalised Ratio was normal. NCCT brain was repeated 24 hours later and showed progression of hemorrhages. It showed progressive worsening of right occipito-temporal ICH, cerebral oedema, midline shift, right SDH and SAH. Patient remained hemodynamically stable and platelet count was on the rising trend. It was 52,000, 77,000 and 83,000 on 3 consecutive occasions. PCV was stable around 43. there have been no other bleeding manifestations neurosurgical interventions weren't attempted and patient was managed conservatively. Amidst maximum care provided, patient succumbed to illness on the subsequent day. It are often concluded that diffused cerebral hemorrhages with moderate thrombocytopenia and normal coagulation profile are a really rare and fatal complication of dengue . Exact pathophysiological mechanism isn't well understood. Increased awareness and high degree of clinical suspicion is required among clinicians for timely diagnosis of this extremely rare complication of dengue . We postulate that immunological mechanisms may play a task in pathogenesis. However further comprehensive research and studies are needed to know the pathophysiological mechanisms resulting in this complication.

Dengue hemorrhagic fever is a severe, potentially deadly infection spread by some mosquitos. The dengue virus is transmitted by mosquitoes. Symptoms of Dengue hemorrhagic fever are fever that lasts from 2 to 7 days, Vomiting blood, Drowsiness, Bleeding from nose or gums. Dengue hemorrhagic fever is caused by a virus for which there is no known cure or vaccine. Only treatment is to treat the symptoms, helping body to heal naturally. Major Research to cure the disease various researches includes means of vector control, vaccine development, and antiviral drugs are going on in Germany Sixty cases meeting the case definition were reported in 2001, and 231 cases were reported in 2002. Case reports rose continuously from 7 cases in the first quarter of 2001 to 82 cases in the second quarter of 2002. In both years, 55% of cases were male. Dengue management algorithms have been developed by the WHO South East Asia Regional Organization (SEARO) and the WHO Pan American Health Organization, which have been further adapted in national guidelines. The premise is distinction of dengue disease from other tropical fevers, for which clinical criteria alone are not sufficiently discriminatory, especially in older adults [22–24]. Diagnostic testing is strongly recommended, summarized in Table 1. In brief, in endemic areas or in likely immune populations with past exposure to dengue or other related flaviviruses, reverse transcription-polymerase chain reaction (RT-PCR) and non-structural protein 1 (NS1) detection are most useful because of

their specificity, particularly in early presentation. In late presentation, clinical manifestations may have to guide management with a battery of repeated tests requiring evidence synthesis by experienced physicians to determine etiology. In travelers or other non-immune populations, in addition to RT-PCR and NS1 in the early or febrile phase, immunoglobulin M and immunoglobulin G may be more useful, but with caveats about accuracy. In the context of an acute undifferentiated tropical fever otherwise negative for common etiologic agents such as *Plasmodium* or *Salmonella*, the combination of leukopenia, severe thrombocytopenia (<50 000/mm^3), rapid changes in hematocrit (>20 % change from baseline or initial value), and elevated transaminases with an asparatate transaminase:alanine transaminase ratio of >1 make dengue the prime candidate. Mild cases that do not reach these values are likely self-limiting or may not benefit from currently available treatment.

Biography

Nayomi Shermila Jayasinghe is working as a Consultant physician in Internal medicine, Bairnsdale Regional Health Service, Victoria, Australia, Associate lecturer of University of Queensland, Ex. Consultant Specialist Physician attached to specialized dengue unit in National Hospital of Sri Lanka. Her main areas of work include – Dengue infection and its complications Author of many publications on dengue infection published in national and international medical journals, symposium and congresses. She has delivered speech on changing trends of dengue infection at World congress of Internal medicine 2018.

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