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Extended Abstract
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Infectious Diseases & Endocrinology 2019: Dengue fever associated cerebral hemorrhages, a rare, poorly understood entity in an era of dengue epidemic: A case series and literature review- Nayomi Shermila Jayasinghe- Bairnsdale Regional Health Service, Australia

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Dengue fever is a tropical disease born of mosquitoes caused by dengue virus. Symptoms usually begin 3 to 14 days after infection. This can involve high fever, headache, vomiting, muscle and joint pains and a skin rash that is characteristic. Recovery takes usually two to seven days. In a small proportion of cases, the disease develops into severe dengue, also known as dengue hemorrhagic fever, leading to bleeding, low blood platelet levels and blood plasma leakage, or into dengue shock syndrome, where blood pressure is dangerously low. Dengue is transmitted by several species of Aedes-type female mosquitoes, primarily A. Egypt. There are five types of the virus; one type of infection usually gives that type lifelong immunity but only short-term immunity to others. Later infection with another type increases the risk of serious complications. Number of tests available to confirm diagnosis, including antibody detection of the virus or its RNA. A dengue fever vaccine has been approved, and is available commercially in a number of countries. As of 2018, the vaccine is recommended only in previously infected individuals or in populations with a high rate of prior infection by age nine. Other prevention methods include reducing mosquito habitat, and limiting bite exposure. This can be accomplished by getting rid of or covering standing water and wearing clothes that cover much of your body. Acute dengue care is compassionate, which involves providing fluid for mild to severe disease either by mouth to intravenously. Blood transfusion can be needed for more serious cases. Each year about half a million people require hospital admission. Paracetamol (acetaminophen) is recommended for fever reduction and pain relief in dengue instead of nonsteroidal anti-inflammatory drugs (NSAIDs), due to an increased risk of bleeding from the use of NSAID. Since the Second World War, dengue has become a global problem and is common in over 120 countries , mainly in Asia and South America. Approximately 390 million people get infected a year, and about 40,000 die. A substantial rise in the number of cases was seen in 2019. Earliest epidemic reports date from 1779. It was recognized by the early 20th century that its viral origin and spread was. Aside from killing the mosquitoes, research is underway on drugs specifically aimed at the virus. This is classed as a neglected tropical disease. People diagnosed with dengue virus are usually asymptomatic (80 percent) or only have mild symptoms such as uncomplicated fever. Others have more severe disease (5 per cent) and it is life-threatening in a small proportion. The period of incubation (time between exposure and onset of symptoms) ranges from 3 to 14 days but mostly 4 to 7 days. Travelers returning from endemic areas are therefore unlikely to have dengue fever if the symptoms start more than 14 days after they arrive home. Children also experience similar symptoms to common cold and gastroenteritis (vomiting and diarrhea) and are at greater risk of serious complications, while initial symptoms are usually mild but include high fever.

Dengue fever is caused by a flavivirus, which is 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 have been reported. Neurological manifestation in dengue hemorrhagic fever usually results from multisystem dysfunction secondary to liver failure, cerebral hypoperfusion, electrolyte imbalance, shock, cerebral edema and hemorrhage related to vascular leak. The occurrence of brain hemorrhage in a case with dengue shock can be serious and leads to death. The occurrence of brainstem hemorrhage can be a very serious fatal situation. We report this case series of dengue hemorrhagic fever with multiple intracranial, sub arachnoid hemorrhages and sub-dural hematoma

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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 time with signs of vascular leakage. She was intubated and ventilated with supportive care. Later on, she developed features of cranial diabetes insipidus and it responded to intranasal desmopressin therapy. In spite of above measures signs of brainstem herniation developed and she 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 did not have evidence of any bleeding Intra Cranial Hemorrhage (ICH) in right parietal lobe deep white matter area associated with perilesional oedema and midline shift. Bleeding into the right lateral ventricle and Small Subdural Hematoma (SDH) were also noted in right parietal 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 were no other bleeding manifestations neurosurgical interventions were not attempted and patient was managed conservatively. Amidst maximum care provided, patient succumbed to illness on the following day. It can be concluded that diffused cerebral hemorrhages with moderate thrombocytopenia and normal coagulation profile are a very rare and fatal complication of dengue fever. Exact pathophysiological mechanism is not well understood. Increased awareness and high degree of clinical suspicion is needed among clinicians for timely diagnosis of this extremely rare complication of dengue fever. We postulate that immunological mechanisms may play a role in pathogenesis. However further comprehensive research and studies are needed to understand the pathophysiological mechanisms leading to this complication.

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