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Spectrum of rare presentation of Dengue viral infection-in Srilanka -A case series and Review of literature

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Abstract: Dengue fever [DF], also known as break-bone fever is a mosquito-borne infection that causes spectrum of clinical manifestation ranges from flu-like illness self- limiting febrile episode dengue hemorrhagic fever [DHF] and dengue shock syndrome [DSS]. It is a major international public health fear due to its rising morbidity and mortality in all age group. Four different viruses can cause dengue fever, all of which are spread by a particular type of mosquito *Aedes aegypti* and *Aedes albopictus*. Irrespective of serotype early management of dengue fever is crucial in order to prevent rare complications. In our clinical practice we have encountered different rare presentation of dengue fever. The first case illustrates dengue with unusually high liver enzymes. Second case reports a young man with intra cerebral hemorrhage. Third case presented with sub acute appendicitis.
Keywords: dengue, hepatitis, intracerebral hemorrhage, liver enzyme SriLanka

INTRODUCTION

Dengue viral fever is endemic in tropical and subtropical areas. Dengue fever is estimated by the World Health Organization (WHO) to cause about 50-100 million infections per year Worldwide [1]. DF and DHF are endemic to Southeast-Asia, Western pacific and Caribbean. It has become a major international public concern particularly in tropical and subtropical regions. Environmental factors including climate changes play a crucial role in the epidemiological pattern of DF and DHF in terms of the number of cases, severity of illness, shifts in affected age groups, and the expansion of spread from urban to rural areas. There is a regular incidence of DF/DHF throughout the year, with the highest incidence during the rainy months [2].

According to the Srilanka epidemiology unit report that first three month of 2017, around 30,000 cases were reported, of that 41.32% were reported from western province [3]. Secondary dengue viral infection is more common in our clinical practice. When compared with primary dengue infection, secondary dengue infection is associated with more severe clinical presentation [4]. It is well-known that secondary dengue viral infection causes serotype cross reactivation among memory T cells which is contributing to severe dengue fever [5]. The situation is more serious in the low-socioeconomic nations which are poorly equipped to control the vector *Aedes aegypti* responsible for spread of infection [6]. As the incidence of dengue increases, incidence of atypical presentations are also on the rise, although these may be under reported because of lack of knowledge and under diagnosis of dengue. A variety of atypical manifestations of dengue have been described [7, 8]. Health alertness among the public regarding the possible nature of dengue virus, actions required in controlling the spread of infection and effective management of infected patients during dengue epidemics and endemics is the need of the hour. This spectrum of case series clearly indicates atypical nature of dengue viral fever.

CASE PRESENTATION

Case 1

A 34 -year-old Srilankan presented to the emergency department with two day history of fever, joints pain myalgia and malaise. He was previously healthy and none evaluated. Third day of fever, he complained of upper abdominal pain and vomiting. Physical examination revealed, ill looking, temperature of 39°C with pulse rate was 98beat/min and Blood pressure was 110/80mmHg.He was haemodynamically stable. His white blood count (WBC) revealed reduced total blood count with neutropenia and progressive declined platelets [WBC-$2x10^9$/l, and platelets-$30x10^9$/l]. Exceptionally, his liver profile revealed very high aspartate aminotransferase (AST-9,800u/l) and alanine aminotransferase (ALT-7400u/l) has been observed in his third day of fever. His platelet counts started to drop further to reach 13x109/l. Fourth day of the fever patient showed clinical evidence of leakage which was confirmed by inward ultrasound. Sixth day of fever both IgM and IgG dengue antibodies became positive, leading to diagnosis of Dengue hemorrhagic fever. Fifth day after the admission, patient felt free from temperature. Interestingly, liver enzyme dropped below 100u/l after sixth day from the day of highest

elevation of liver enzymes. Patient was discharged, 10th day after admission.

DISCUSSION

Spectrum of liver involvement was seen in dengue fever, it ranges from asymptomatic liver enzyme elevation to fulminant hepatic failure. Microscopically, this comprises fatty changes, hepatic necrosis, hyperplasia and destruction of Kupffer cells. Liver involvement is more common and more severe in children as compared to adults [9]. High level of viral load is associated with more severe disease and organ involvement especially liver [4]. Liver derangement mainly due to two mechanisms, one direct dengue viral infection secondly, deregulated immunologic injury. These two modes of liver involvement shows wide spectrum of manifestation from asymptomatic elevation of liver enzyme to severe form of acute liver failure [9].

On third day of fever, this patient complained of abdominal pain and vomiting. Initially we suspected leakage in to the peritoneal cavity. Liver scan revealed evidence of free fluid in the peritoneum and pleural space. Same day liver profile showed very high AST (>9800) and ALT (>7400) with mildly elevated serum bilirubin. Most of the available data revealed that in the case of dengue fever elevation of AST is more than ALT; this pattern is more during the first week of infection. But liver enzymes come back to normal within three weeks of time. It could be partially explained that dengue viral infection primarily involved in the muscle satellite cells [10]. The AST released from damaged myocytes could be explained for the elevation of AST than ALT. Elevated AST and gamma glutamyl transferase (GGT) indicates more severe disease [11].

We also could suspect that this high level of transaminase level can be seen in anoxic hepatic injury, where we are able to observe massive and rapidly reversible increase transaminase level [12]. Another clue to think about anoxic hepatic injury is that transaminase elevation more than 20 fold from the base line [13]. In this case high level aminotransferase level come back to near base line within a week period and initial aminotransferase level more than 20 fold of increase from the baseline, all of the facts indicate that some elements of anoxic hepatic injuries happened. This could be due to poor perfusion of liver due to dengue leakage.

Case 2

A 23 year old young man transferred from the local hospital to the Teaching hospital Batticaloa emergency department with the history of fever and myalgia and joints pain for three day duration. He was previously well with no history of recent travel to any endemic area visit. He has not complained of abdominal pain, headache and vomiting. Third day after the admission, he became ill and complained of severe headache and vomiting. Physical examination revealed, patient was drowsy temperature 39.C, and slightly dehydrated. His tourniquet test was negative, full blood count(WBC-3x19^9/l), packed cell volume(45%), liver profile(AST-54u/l,ALT-46u/l) and renal functions(BU-7mmol/l) .Dengue IgM antibody confirmed that this patient had dengue fever. Sixth day after admission, patient conditions get worse and latest platelets come down to 14x10^9/l with haematocrit of 49% and a normal white cell count. Liver enzyme was increased threefold. Patient's level of conscious around [GCS] 8/15.We arranged immediate non-contrast brain CT-scan, which revealed right sided large intracerebral hemorrhages with midline shift. Two days later patient passed away.

DISCUSSION

Neurological complications are rare in comparison with other complications. There are spectrum of neurological presentations were reported in the literature, varied from aseptic meningitis, encephalitis, encephalopathy, Guillain–Barre syndrome, intracranial hemorrhages, thrombosis, mono neuropathies and polyneuropathies [14].

Dengue fever with diffuse cerebral hemorrhages is one of the rare complications. This internal bleeding mainly due to low platelets [14]. This phenomenon has been reported several instances, but there was no correlation between degree of thrombocytopenia and bleeding manifestation [15]. Some study has been noted that those who had dengue IgG antibody positive are vulnerable to develop dengue related hemorrhagic manifestations[16]. Neurological complications are more pronounced in secondary infection than primary infection. There are several factors contributed to bleeding in dengue fever but still unclear, some researchers believe vasculopathy play major role than thrombocytopenia. When intracerebral bleeding developed in dengue fever, there is no study showed that large amount of platelets or fresh frozen plasma would change the outcome. An article published in 2011, which revealed that prophylactic platelets transfusion leads to more detrimental effects than beneficial effects [16] based on the available study, timely needed neurosurgical intervention will save some extend. However, before surgery platelets transfusion is mandatory [14].

Case-3

A 15-year old boy admitted to medical ward with the history of abdominal pain and fever for 3 days duration. Initially he had fever with myalgia and joints pain. He had abdominal pain at peri-umbilical region. On examination, he was dehydrated and tenderness on the right iliac region .His fever was persisted for last 5 days duration. Abdominal ultrasound revealed sub acute appendicitis. His blood report revealed that reduced total count (1.2x10^9/l) with lymphocyte predominant. Surgical opinion was taken, but surgery was given up due to dropping platelets (10x10^9/l). Dengue viral fever

was diagnosed with positive IgM and IgG antibodies. His platelets started to drop and reached 10,000/cm^3 at 5 day after admission. We arranged second abdominal scan two days later which revealed inflamed appendix with fluid collection in the paracolic region and also right sided pleural effusion was noted. At this juncture, we made diagnosis as dengue hemorrhagic fever. Interval appendicectomy planned and empirical antibiotic started. Patient improved day by day and platelets started to rise.

DISCUSSION

Symptom of abdominal pain is a common presentation of dengue fever. Spectrum of causes for this abdominal pain varies from mesenteric adenitis, hepatitis, dengue hemorrhagic fever, lymphoid hyperplasia, acalculus cholecystitis, acute pancreatitis and appendicitis [17]. Because of minimal symptoms and signs for appendicitis, diagnosing appendicitis is challenging for physicians and surgeons [18]. In the case of appendicitis we would like to expect increased full blood count with neurophil leucocytosis. However, this patient's platelets started to drop it would suggest that this patient had dengue viral fever. The incidence of acute abdomen in dengue fever has ranges from 4.3% to 12.04% [18]. Early detection of dengue viral fever is difficult in most part of the Sri Lanka because of unavailability of the antigen test in the government health sector. Repeated and more frequent clinical assessment is important to a prevent acute appendicitis. Indication for appendicitis in case of dengue is real challenging, but may consider surgery if persistent fever with right iliac fossa tenderness, evidence of peritonitis and leucocytosis [19]. According to the guideline, surgery can be done if platelets count more than $50x10^9$/l [20].

CONCLUSION:

Dengue fever had wide spectrum of clinical presentation. Early detection of dengue fever is mandatory and regular monitoring and early management will prevent the development of complications.

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Conflict of interests No conflict of interests is declared.

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