

## Case Report

# Dengue Associated Multiple Organ Failure

**Eric Martinez\***, Virginia Capó

Department of Teaching, Institute of Tropical Medicine, Pedro Kourí, Autopista N, Cuba

\***Corresponding author:** Eric Martinez Department of Teaching, Institute of Tropical Medicine, Pedro Kourí, Autopista N, Cuba

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## Abstract

Dengue is a disease caused by an arbovirus, which has four related virus serotypes and is currently the most important mosquito borne viral pathogen affecting humans, emerging as a major threat to global health. Dengue is a systemic and dynamic infectious disease that includes shock hemorrhage and organ impairment. Multiple Organ Failure (MOF) which usually but not always is a consequence of prolonged or recurrent shock. Two clinical cases are presented and analysed.

**Keywords:** Dengue; Multiorgan Failure; Pathology Findings

Dengue is a disease caused by an arbovirus, which has four related virus serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) and is currently the most important mosquito borne viral pathogen affecting humans, emerging as a major threat to global health [1]. Its incidence has increased more than 30-fold in recent decades alongside the geographical expansion of the *Aedes* vector mosquitoes. It is estimated that 3 billion people live in areas at risk of contracting dengue and some 390 million infections (96 million symptomatic) and 20,000 deaths from dengue occur every year [2], in the endemic regions [3].

Dengue is a systemic and dynamic infectious disease [4]. The infection may be asymptomatic or presents itself with a broad clinical spectrum that includes both severe and non-severe clinical manifestations [5], for which the timing or sequence of infections can be an important determinant of disease severity and course [6]. Severe Dengue includes Multiple Organ Failure (MOF) which usually but not always is a consequence of prolonged or recurrent shock [7].

## Dengue Classification

Dengue illness is clinically classified as either dengue with or without warning signs or severe dengue. This classification was launched by the WHO in 2009 for the purpose of improving clinical management [8]. The warning signs permit the early identification of patients with more severe disease manifestations who require supportive therapy [9]. This classification has substituted the previous 1997 WHO system that addressed and underscored the two pathological phenomena, plasma leakage and abnormal haemostasis, associated with the disease [10]. Under this classification, patients were designated as having either Dengue Fever (DF) - a non-specific febrile illness and the most common manifestation of DENV infection - or Dengue Haemorrhagic Fever/Dengue Shock Syndrome (DHF/DSS) - a combination of plasma leakage and coagulopathy, sometimes accompanied by bleeding, that can lead to a rapid fall in blood pressure and consequently to circulatory shock and organ impairment [11].

## Severe Dengue

Every dengue case that has one or more of the following manifestations [12]:

a) shock or respiratory distress due to severe plasma leakage:

shock evident from tachycardia, cold extremities, and capillary refill time equal to or greater than three seconds, weak or undetectable pulse, convergent/ differential blood pressure  $\leq 20$  mmHg; arterial hypotension in late phase.

b) Severe bleeding based on evaluation by the attending physician (e.g. hematemesis, melena, ample metrorrhagia, and central nervous system bleeding).

c) Severe organ involvement, such as major liver (AST or ALT  $>1000$  IU), central nervous system [13,14], heart [15,16], or kidney [17,18] impairment.

## Multi-Organic Dysfunction Syndrome (MOD)

MOD associated to Severe Dengue has been described mainly in children but also in adults, usually associated to Shock [19]. Young girls with MOD have been described by Salgado et al [20]: after 4 days of fever they had shock resistant to usual treatment with crystalloids and colloids with tachycardia, ventricular arrhythmia, increased CPK MB, AST and ALT, coagulopathy with prolonged PTT and PT but without severe thrombocytopenia, metabolic alteration with acidemia and hypoglycemia. Score for MOD proposed by Leteurtre S, et al [21], was applied with an average of 23 and evidence of myocardial, hepatic and hematological major compromise. Dengue 3 was showed by RT-PCR.

DOM has been described as a progressive dysfunction of two or more organs or systems after an acute alteration of systemic homeostasis [22]. Alterations in liver, heart, nervous and hematologic systems have been associated to DOM in patients with Severe Dengue [23]. Risk factors predisposing DOM have been also described, including inflammatory (malaria, hepatitis y tuberculosis, among others) and no inflammatory conditions, as well as activation of innate immune system [24]. Scores for prognostic classification have been developed [21]. Some particular DENV strains have been associated to DOM [25].

## Here We Present Two Adult Cases of Dengue Associated MOD

### Case presentation

**Case 1:** This is a ninety two years old patient with previous right

nephrectomy due to lithiasis. He was admitted on September 1st and died on September 4th. Three days previous to hospital admission he started with high fever, head and eye aches, nausea and vomiting. On the first day as inpatient he presented epigastric pain, asthenia, anorexia, loose stools. The next day he suffered marked fatigue. Abdominal ultrasonographic exam was normal. Hemoglobin figures started to diminish from day one with 111 g/L to 78 g/L, BUN 206, AST 67 the day he dies. Hematocrit from 33% moved to 24%. He had bloody stools and red blood was obtained from the stomach and received blood transfusion but eventually he died. Clinically was interpreted as a hypovolemic shock due to gastrointestinal bleeding during dengue infection. Autopsy findings concluded that two chronic peptic penetrating ulcers found in duodenum were the source of the massive upper GI tract bleeding in the course of DENV 3 infection as corroborated by the virology lab. Focal necrosis of hepatocytes, edema of the GI tract walls, as well as disseminated echimoses on the visceral pleura, associated with the shock syndrome, was found.

**Case 2:** A 25 y. o. previously healthy man except for a sickle cell trait (Hemoglobin SA) started with high fever, headache, vomiting, arthralgia, loss of appetite and general malaise. Three days before admittance in the hospital on November 24th his blood tension lowered to 100/70, and showed increasing Hematocrit up to 48% and decreasing platelet counts (120 000X10<sup>9</sup>-35 000X10<sup>9</sup>). He refers hematuria, one vomit, severe abdominal pain, and says that he feels uneasy.

Clinically the case was interpreted as severe dengue and was treated according to WHO (WHO/TDR, 2009) indications with saline solutions trying to avoid a shock syndrome due to capillary leakage associated with DENV infection. Despite all the efforts to avoid the shock the patient died two days after admission. Autopsy findings were concluded as a severe DENV 3 infection with shock syndrome with internal fluid evasion into peritoneal (1 500ml) and pleural cavities (200 ml each), into intraperitoneal tissues such as visceral serosa and walls of abdominal organs (intestines, gallbladder), sub endocardicechymoses on the left ventricle, sickle cell formation of intravascular erythrocytes, as well as generalized visceral blood congestion and other minor findings not related with shock.

## Discussion

In the presented cases severe dengue was associated to plasma leakage and haemorrhage that lead to shock syndrome. Shock syndrome was irreversible for both cases. Functional impairment of liver and kidney were biochemically detected but since the patients did not survive long enough in shock, morphological manifestation of hepatic or kidney damage were not so evident. However, echimotic lesions in the endocardium may be found in dengue cases with shock.

In Case one, Dengue infection determined the GI tract hemorrhage from the inactive chronic ulcers and became the cause of the intractable bleeding. In Case two, a severe plasma leakage into visceral organs and pleural and peritoneal cavities produced a progressive shock associated to dengue infection. Sickle cell trait probably contributed to the fatal evolution of this case as described elsewhere.

## Conclusion

Dengue shock syndrome due to plasma leakage and/or hemorrhage

may be fatal, in association with multi organ involvement.

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