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Case Report

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Critical Care Management in Dengue Shock Syndrome with Acute Kidney Injury

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ABSTRACT

Renal failure is a potential complication that can occur in severe dengue infections. It typically affects 2-5% of cases and is associated with a high mortality rate. This case report presents a middle-aged female with dengue shock syndrome and co-existing urosepsis resulting in acute renal injury requiring intensive care management. The case report highlights dengue fever, in the manifestation of dengue shock syndrome, as an exacerbating factor for acute kidney injury in a patient at risk of kidney injury with a coexisting bacterial infection.

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Introduction

Dengue can be found in more than one hundred countries throughout the globe, with approximately forty percent of the world's population living in areas at risk for the contraction of dengue fever [1,2]. Dengue is a vector borne disease transmitted mainly through the bite of an infected Aedes species, either Aedes aegypti or Aedes albopictus, mosquito. Dengue fever has four serotypes and infection with anyone can result in patients having either no symptoms, classic dengue fever, dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) (1). The following case report is that of a middle-aged female, with a history of nephrolithiasis, who presented with primary complaints of right sided abdominal pain and subjective fever. She also revealed that she was experiencing headaches, vomiting, urinary frequency, urgency and urinary incontinence. After a full history, examination and laboratory and radiologic investigations, she was diagnosed with DSS and co-existing urosepsis resulting in acute renal injury requiring intensive care management. The case report highlights dengue fever, but in particular DSS, as an exacerbating factor for acute kidney injury (AKI) in a patient at risk of kidney injury with a coexisting bacterial infection.

Case Report

A 46-year-old female, with a known history of nephrolithiasis, presented to the emergency department with complaints of subjective fever for the preceding two days and right sided abdominal pain for the preceding seven days. She had associated symptoms of headaches, vomiting, urinary frequency, urinary incontinence and a rash to the upper limbs and thighs. The patient admitted to having similar rashes to the skin previously and explained the causative agent to be mosquito bites. The patient was known to have a history of nephrolithiasis and initially attributed the abdominal pain to this as she had passed three renal calculi four days prior to hospital presentation. However, pain cessation did not occur following the passage of the renal calculi. The patient denied any myalgia, arthralgia or retro-orbital pains. There was also no sick contacts or history of recent travel. The patient's body mass index (BMI) was calculated at 28.4 kg/m2. No other co-morbidities were noted.

On physical examination, the patient was noted to be tachypneic, tachycardic and hypotensive. However, she was afebrile at time of examination. Normal heart sounds were appreciated with no murmurs identified, and her capillary refill time was within normal limits. Auscultation of her lungs revealed no abnormalities. The abdomen revealed hepatomegaly with right sided abdominal tenderness and right sided renal angle tenderness. There were no focal neurological deficits identified. She was alert and oriented to time, place and person. There were no signs of meningeal irritation and pupils were equally reactive to light.

Chest radiograph showed hazy bi-basal infiltrates with blunting of costo-phrenic and cardio-phrenic angles. Electrocardiogram demonstrated sinus tachycardia of 120 beats per minute. Blood gas analysis revealed a type 1 respiratory failure (PCO_2 of 27 mmHg, PaO_2 of 59 mmHg) and metabolic/lactic acidosis (pH 7.254, HCO_3 of 11 mmol/l, base excess of -15 and lactate of 2.4 mmol/l). Infectious parameters showed a leukocytosis (14 x 10^9/l) and thrombocytopenia (80 x 10^9/l) and elevated c-reactive protein (CRP) (217.3mg/l). Liver enzymes were mildly deranged including bilirubin and creatinine was also elevated (2.8 mg/dl). Dengue infection was confirmed by positive Immunoglobulin M

(IgM) and Immunoglobulin G (IgG) antibodies on serum viral studies. The patient was intubated, mechanically ventilated and invasively monitoring in the intensive care unit (ICU).

Core temperatures ranged from 35°C to 39.3°C from days one to four of ICU admission. Mean arterial pressures of 65- 90 mm Hg with pulse pressures of 30 – 40 mmHg were noted on admission. Early goal directed fluid resuscitation was used to maintain central venous pressures between 10- 18 cmH20 factoring in a positive end-expiratory pressure (PEEP) ventilatory setting of 5 cm H20. Inotropic support was implemented to maintain mean arterial pressure (MAP) > 65 - 75mmHg. Microbiologist guided empiric antibiotics and multidisciplinary surgical and medical intervention also formed part of the ICU management. A diagnosis of co-existing urosepsis was entertained following microbiological identification of Escherichia coli in the urine upon presentation. Abdominal ultrasound and computed tomography (CT) scan yielded the evidence of a right ureteric renal calculi and early abscess formation leading to hydronephrosis. An open right ureterolithotomy was performed which allowed drainage of purulent material. Following this intervention, the patient made significant improvements including resolution of her sepsis with subsided temperature spikes, down trending inflammatory mediators including leucocyte count and CRP to baseline lab investigations. The ventilatory parameters were weaned and the patient was extubated on day seventeen of ICU stay. The serum creatinine also returned to normal baseline values without need for renal replacement therapy.

Discussion

Dengue is a mosquito-borne viral infection, found mainly in the tropical and sub-tropical climates worldwide. Most dengue infections produce only mild illness of flu-like symptoms, but it may develop into severe illness with potentially fatal complications. Global incidence of dengue has increased dramatically in recent decades with an estimated 100 to 400 million infections yearly [1]. Dengue is transmitted to humans from the bite of an infected Aedes mosquito primarily, but there has been incidence of vertical transmission during childbirth.

In the year 2015, there were over 4000 deaths due to complications, a four-fold increase from the year 2000. In the Americas, in 2019, there were over 25000 severe cases with complications [1]. The first reported case of DHF and DSS in Trinidad and Tobago was in 1997 [3]. The infection was confirmed using clinical suspicious as well as serological diagnosis in five patients. Three developed DSS which proved fatal while those who had DHF survived.

Dengue can be suspected when a high fever (40°C) presents with any of the following two symptoms: severe headache, retro-orbital pains, myalgia, arthralgia, nausea, vomiting, rash hemorrhagic manifestations and leukopenia. However, given the varied clinical presentation that occurs with dengue illness, clinical definition alone is not appropriate, laboratory confirmation is emphasized [1]. Confirmatory supportive serology such as enzyme – linked immunosorbent assay (ELISA), positive antibody IgM testing and isolation of the dengue virus from serum can be used. Additionally, dengue can also be confirmed using detection of the viral genome sequence in cerebrospinal fluid using polymerase chain reaction (PCR).

Severe dengue normally may occur three to seven days after the onset of illness and is a potentially fatal complication which can lead to DHF and DSS. DHF is characterized by: i) fever or history of acute fever lasting two to seven days occasionally biphasic, ii) hemorrhagic tendencies such as positive tourniquet test, petechia, ecchymoses, purpura, bleeding mucosa or injection sites, hematemesis or melena, iii) thrombocytopenia (< 100 x 10^9) and iv) evidence of plasma leakage due to increased vascular permeability must also be present [1]. Evidence of plasma leakage can manifest with an increase in hematocrit to greater that 20% above average, decrease in hematocrit following volume replacement to greater than 20% of baseline or signs of plasma leakage such as pleural effusions, ascites and hypoproteinemia. In DSS, four criteria of dengue hemorrhagic fever must be present and there must be clinical signs of circulatory failure including rapid weak pulse and narrow pulse pressure (< 20 mmHg) [1]. It can also be manifested by age related hypotension and cold, clammy skin and restlessness.

The diagnosis of DSS was considered in this patient following a confirmed positive antibody IgM test, biphasic fever, thrombocytopenia (80 x 10^9/l), bleeding tendencies as evidenced by haematuria, evidence of plasma leakage by bilateral pleural effusions on chest x-ray and haemodynamic instability as evidenced by tachycardia and inotropic requirements despite fluid resuscitation .Although biphasic fever is a known manifestation of dengue fever , it has similarly been reported in bacterial infections and could also have been a manifestation of the Escherichia Coli associated urosepsis in this patient [4,5]. We postulate that the synergistic effect of viral and bacterial co-infection induced an inflammatory response that worsened and resulted in AKI in this patient.

The Kidney Disease Improving Global Outcome (KDIGO) working group clinical practice guidelines defines AKI as any of the following: an increase in serum creatinine by 0.3mg/dl from baseline within forty-eight hours, an increase of 1.5 times the baseline within last seven days or urine volume of <0.5 ml/kg/ hour for six hours [6]. In keeping with these criteria our patient was considered Stage 3 AKI based on an estimated 3-fold rise in serum creatinine levels to 2.8 mg/dl from a baseline of 0.8mg/dl in the first 48 hours and a reduced urine output of less than 0.5ml/kg/hr for more than 12 hours. The AKI-EPI study reported AKI in up to 50% of critical care patients and noted that AKI severity in the critical care setting is associated worsened morbidity as reflected by worsening kidney function upon hospital discharge [7]. Although multifactorial, AKI precipitating factors were attributed to hypovolemia, nephrotoxic drugs and sepsis.

A retrospective study among dengue patients reported a 14.2% incidence of AKI and identified independent predictive factors for developing AKI including DHF, multiorgan dysfunction and Diabetes Mellitus [8]. Although in comparison to other reports this high incidence may be reflective of sampling from a dengue "hotspot" in an endemic county, similar associated factors including severity of dengue fever, older age group, obesity, coexisting bacterial infection and hypoalbuminemia on admission have been noted [9]. Dengue should be considered a major contributor to the development of AKI among patients where the infection is endemic and the prevalence is greater. Urinary tract obstruction due to renal calculi leads to urinary stasis and predisposes to urosepsis. DSS is a severe form of presentation of the infection which when paired with coexisting bacterial infection increased the risk for developing AKI in this patient [10]. Escherichia Coli contributes to up to 50% of urosepsis and like other bacteria generates a complement mediated inflammatory response and nitric oxide induced injury to endothelial tissue [11]. The haemodynamic instability that accompanies DSS induces a systemic inflammatory response mediated endothelial tissue injury

while dengue viral antigen induced antibodies also injure renal tissues and further compromises renal perfusion leading to AKI [11]. The elevated BMI of 28.4 kg/m^2 could also be considered a risk factor for development of AKI.

The improved renal outcome following surgical intervention was attributed to source control following ureteric lithotomy which removed the nidus of infection and attenuated the systemic inflammatory response. Additionally, relief of the hydronephrosis reduced the mechanical pressure on the kidney contributing to AKI. The management of DSS focused on respiratory support by mechanical ventilation to reduce the work of breathing and cardiovascular support with fluid resuscitation and use of inotropes. The combined approaches restored haemodynamic stability and reduced kidney injury allowing the patient to recover with improved respiratory and inflammatory parameters without the need for renal replacement therapy or progression to chronic kidney disease.

Conclusions

DSS and co-existing urosepsis contributed to the development of AKI in this patient. Pathophysiological mechanisms common to both disorders include inflammatory mediated endothelial injury and direct renal cytotoxic effects. Successful source control via surgical intervention and supportive care in the management of DSS reduced the systemic inflammatory response, improved renal function and avoided the need for renal replacement therapy. This case further supports the need for early detection and aggressive intervention towards AKI in the critical patient.

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Conflict of Interest – None to declare.

Informed Consent Statement – Informed consent was obtained from the patient.

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