CASE REPORT

Rhabdomyolysis and acute kidney injury in dengue fever

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SUMMARY

Rhabdomyolysis is a rare but potentially lethal complication of severe dengue fever. We present a case of 21-year-old man with fever, bodyache and black coloured and decreasing amount of urine. He was positive for NS₁ (non-structural protein-1) antigen and IgM antibody for dengue. Platelet count was below $20 \times 10^9/L$ and kidney function test was deranged. Urine was positive for myoglobin. The patient was managed emergently on conservative lines and improved in 10 days. Rhabdomyolysis should always be kept in mind in a patient with severe dengue, as its early detection and prompt management can prevent further progression to acute renal failure.

BACKGROUND

Dengue fever is caused by a virus, known as dengue virus, from the genus *Flavivirus*. Although the virus is responsible for a variety of regularly seen complications, including dengue haemorrhagic fever (DHF), dengue shock syndrome (DSS), liver failure and disseminated intravascular coagulation, rhabdomyolysis is observed uncommonly. It leads to the release of muscle protein myoglobin in the bloodstream, which is harmful to the kidneys and leads to the development of renal failure. We describe an interesting case of dengue fever presenting with rhabdomyolysis leading to acute kidney injury.

CASE PRESENTATION

A 21-year-old man presented to our emergency department with moderate to high-grade fever for the past 4 days, generalised bodyache for 3 days and black coloured urine for the past 1 day. He also reported a decreasing amount of urine output for the past 3 days, which, after admission, was measured at 600 mL over the following 24 h. There was no bleeding anywhere on the body. He did not suffer from any systemic disease and only took paracetamol 500 mg tablets on and off to control the fever. No other drugs were reported given prior to hospitalisation.

On arrival, the patient's recorded oral temperature was 38°C, pulse rate, 100 bpm, respiratory rate, 16 breaths per minute, blood pressure, 120/84 mm Hg and SPO₂ was 98%. On systemic examination, the cardiovascular system had normal heart sounds and no murmur; in the respiratory system, the chest was bilaterally clear; abdominal and neurological examination also revealed no abnormality.

INVESTIGATIONS

Laboratory values disclosed that the patient's peripheral white cell count was $3.4 \times 10^9/L$ with 80%

polymorphonuclear cells, haemoglobin, 11.3 g/dL, haematocrit, 51%, platelet count, $18 \times 10^9/L$, prothrombin time, 12.5 s, international normalised ratio, 1.09, serum sodium, 139, serum potassium, 4.1, serum urea, 62.38, serum creatine, 2.7, serum bilirubin (total 0.86 and direct 0.28), aspartate aminotransferase (AST), 2786 U/L, alanine aminotransferase (ALT), 956 U/L, serum albumin, 3.5 g/dL, serum lactate dehydrogenase (LDH), 890 U/L and creatine phosphokinase (CPK MM) was 7800 U/L. The patient was found to be positive for non-structural protein-1 NS1 (non-structural protein-1) antigen. His blood culture report was sterile. Urine examination was positive for myoglobin and protein (800 mg%), but negative for porphobilinogen, haemoglobin and red blood cells. Twenty four hour urine protein examination revealed 5818.5 mg of protein. Thick and thin smear for malaria, and serological test for malaria and typhoid, were negative. Serological test for leptospira was negative. A posteroanterior view chest X-ray revealed clear lung fields. ECG was normal. A diagnosis of dengue fever leading to rhabdomyolysis, resulting in renal impairment, was performed.

DIFFERENTIAL DIAGNOSIS

- ▶ Acute intravascular haemolysis in malaria (Blackwater fever)
- ▶ Acute glomerulonephritis
- ▶ Porphyria
- ▶ Paroxysmal nocturnal haemoglobinuria

TREATMENT

The patient was managed conservatively. He was given half normal saline (0.45% saline) along with 75 mmol of sodium bicarbonate. The sodium bicarbonate was given to increase myoglobin solubility and to prevent its precipitation in the renal tubules. The patient was subjected to strict monitoring of vitals and serum electrolytes, and regular intake-output measurement.

OUTCOME AND FOLLOW-UP

Platelet count rose to $34 \times 10^9/L$ on the third day of hospitalisation. Kidney function tests were repeated every alternate day and serum creatinine was found to be in a decreasing trend: 2.4 on day 3, 1.9 on day 5, 1.6 on day 7 and 1.2 on day 9. AST and ALT values were also showing a decreasing trend. On repeated testing, on day 4, values recorded were AST 1531 U/L and ALT 402 U/L followed by AST 532 U/L and ALT 167 U/L on day 9. On the fourth day of hospitalisation, IgM antibody for dengue was sent and found to be positive.

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CPK-MM reduced to 1580 U/L, serum LDH reduced to 354 U/L and urine was found negative for myoglobinuria on the ninth day. Urine output improved to 1800 mL/24 h on the sixth day of admission. The colour of the urine also turned from a deep black, as observed on the day of admission, to yellow. Platelet count improved to $110 \times 10^9/L$ as observed on the same day. Having closely observed the patient's constant improvement in lab parameters and also the fact that he remained clinically stable, he was discharged on ninth day. On his next visit 7 days later, he was asymptomatic and his laboratory parameters had settled down to close to normal levels. Urine output continued to be satisfactory.

DISCUSSION

Dengue fever is a mosquito-borne disease caused by any of four serotypes of dengue viruses (serotypes 1, 2, 3 and 4). Symptoms include high-grade fever, severe headache and bodyache, pain behind the eyes and skin rashes. Usually, it runs a self-limiting course in patients infected for the first time. Patients with an earlier history of dengue fever can develop serious complications, including DHF, DSS, liver failure and disseminated intravascular coagulation. Uncommon complications of dengue infection include mononeuropathies, polyneuropathies, encephalitis, Guillain-Barre syndrome and myocarditis.^{1 2} We have reported on another infrequent complication of dengue fever, rhabdomyolysis. There are a limited number of similar cases reported with reference to acute kidney injury in patients of dengue fever. In one such study, incidence of complicated renal dysfunction was reported to be 0.3% in patients of DHF.^{3–11}

The suggested pathogenesis of rhabdomyolysis can be related to either direct cytotoxic effect of the virus over muscle fibres or due to the myotoxic effect of cytokines (tumour necrosis factor) released in the body during viral infections. However, the exact pathogenetic mechanism is not clear.^{3 6}

Rhabdomyolysis leads to release of muscle protein and myoglobin, in the blood stream. Myoglobin is deposited along the renal tubules and precipitates after interacting with Tamm Horsfall protein in presence of acidic urine leading to tubular obstruction. Other suggested mechanisms for nephrotoxicity in rhabdomyolysis are direct and ischaemic tubular injury and intrarenal vasoconstriction.¹²

A patient of dengue fever can present with or without warning signs. Warning signs include abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy, restlessness, liver enlargement greater than 2 cm and increase in haematocrit concurrent with rapid decrease in platelet count. Fluid therapy is the mainstay of management of dengue fever. According to WHO guidelines (2012) for clinical management, dengue fever without warning signs can be managed by adequate oral fluid replacement and bed rest. Patients with warning signs or severe dengue need to be managed by parenteral intravenous colloid or crystalloid fluid replacement to prevent shock. Water and electrolyte balance monitoring is a key factor in management and prevention of complications of dengue fever.^{13 14}

Although kidney biopsy was an option in our case, to evaluate likely pathogenic mechanisms and resultant histopathological changes due to dengue fever along with exclusion of other renal

causes as mentioned in some case reports, it could not be carried out due to strong refusal by the patient's attendants.¹⁵

Learning points

- ▶ Among the many complications of dengue fever, it is very important to look for rhabdomyolysis, which presents as dark coloured and reduced urine output.
- ▶ Rhabdomyolysis can be a potentially lethal complication as it can lead to acute kidney injury resulting in acute renal failure.
- ▶ Rhabdomyolysis should be adequately investigated and CPK-MM (creatinine phosphokinase) should be added to the list.
- ▶ An early investigative assessment of renal injury is mandatory as a timely intervention can prevent progression to renal failure.
- ▶ Crystalloid/colloid parenteral fluids are the mainstay in the management of dengue fever. Monitoring of water and electrolyte balance is mandatory to prevent complications.

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