

Acute Kidney

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Acute Kidney Injury in Non-Shock Dengue Hemorrhagic Fever Patient

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Abstract

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Introduction: Acute kidney injury (AKI) is one of the severe complications in dengue hemorrhagic fever, usually occurred in shock. We report an interesting case of AKI in a hemodynamically stable dengue hemorrhagic fever patient.

Case presentation: An 18-year-old male dengue fever patient referred to our institution in his day eight of illness due to three days of decreased urine output. He was hemodynamically stable with thrombocytopenia, increase in creatinine, positive for Anti dengue IgM, proteinuria, and hematuria. Ultrasound examination showed ascites. He was diagnosed with AKI stage III related to dengue hemorrhagic

fever and underwent hemodialysis. A total of four series of hemodialysis and furosemide drip were performed during 12 days of admission and he was finally improved.

Conclusion: Renal injury might occur in hemodynamically stable dengue hemorrhagic patients. It is a reversible condition; hence, appropriate treatment and close monitoring result in good outcomes.

Keywords: acute kidney injury, dengue hemorrhagic fever, dengue infection, stable hemodynamic

Introduction

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Dengue is a major public health problem among tropics and sub-tropics countries. Over the recent five decades, there was a continuously sharp increasing of dengue hemorrhagic fever annual incidence in Indonesia, starting from 0.05 cases per 100,000 person-years in 1986 to 77.96 cases per 100,000 person-years in 2016. Both *Aedes aegypti* and *Ae. albopictus*, main mosquito vector species of dengue virus, are endemic almost in all regions in Indonesia. It has a wide spectrum of clinical manifestations that range from mild flu-like illness to severe forms of hemorrhagic fever and shock. Renal failure is one of the most common atypical manifestations in dengue which is usually due to shock, hemolysis, or rhabdomyolysis.¹⁻⁵

We present an interesting case of acute kidney injury (AKI) in stable hemodynamic of dengue hemorrhagic fever patients with no sign of hemolysis or rhabdomyolysis.

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Case presentation

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This is a case of an 18-year-old Indonesian male patient presented with three days gradually decreased in urine output after one-week admission in a regional general hospital due to dengue fever since one day prior to hospitalization. He had no complaint of massive vomiting, bleeding, or muscle cramp. His blood pressure was 20/80 mmHg with no medical support, heart rate was 80 bpm, respiratory rate was 20 per minute, and body temperature was 37.5°C. He has no medical history of diabetes mellitus, hypertension, cardiovascular disease, kidney stone, or long term analgesic consumption. His urine output was decreased from 600cc/day to 200cc/day. The intravenous fluid was administered appropriately. Laboratory examination showed hemoglobin 16.1 g/dl (NV 12.0-16.0), hematocrite 44.9%, thrombocytopenia $35 \times 10^9/L$ (NV 150-450 $\times 10^9$), increased in creatinine 15.9 mg/dl (NV 0.6-1.2), and proteinuria (+3). No nephrotoxic drug was given during the hospitalization. Therefore, he was referred to our institution.

Physical examination was essentially normal except petechiae on the skin. Laboratory examination results on the first day of admission in our institution (day eight of illness) were as follow: hemoglobin: 16.0 g/dl (NV 12.0-16.0), hematocrite 46.4%, leucocyte: $3.56 \times 10^9/L$ (NV 4.5-11 $\times 10^9$), thrombocyte: $52 \times 10^9/L$ (NV 150-450 $\times 10^9$), urea 237 mg/dl (NV 10-50), creatinine: 19.49 mg/dl (NV 0.6-1.2), sodium: 125 mmol/L (135-145), potassium: 5.8 mmol/L (NV 3.5-5.0), AST: 177 U/L (NV 10-40), ALT: 671 U/L (NV 7-56),

Anti-dengue IgM (+), anti-dengue IgG (-), HbsAg (-), anti HCV (-), anti HIV (-). Urine examination showed protein +3, erythrocyte +2. Abdominal ultrasound revealed ascites and no abnormality in the kidneys and urinary tract. He was diagnosed with AKI stage III related to dengue hemorrhagic fever. He then underwent hemodialysis. On day three of admission, he was hemodynamically stable with oligouria. Laboratory result showed hemoglobin: 12.9 g/dl (NV 12.0-16.0), hematocrite 36.6%, leucocyte: $3.80 \times 10^9/L$ (NV $4.5-11 \times 10^9$), thrombocyte: $75 \times 10^9/L$ (NV $150-450 \times 10^9$). (Figure 1) He got furosemide drip and hemodialyzed for the second time. His urine output gradually improved and reached polyuria phase. Furosemide drip was discontinued on day-10. His serum urea and creatinine were decreased (150 mg/dl and 6.43 mg/dl, respectively). After 12 days of admission and underwent a total of four sessions of hemodialysis, he finally was discharged. (Table 1) He came to the clinic in the next two weeks with no clinical symptom, normal urine output (around 1,500 cc /day), normal serum urea, creatinine, AST, ALT (41 mg/dl, 1.3 mg/dl, 54 U/L, 47 U/L, respectively), and no proteinuria.

Discussion

Dengue infection has continuously become annual public health problem in Indonesia since it was first reported in 1968. It might be clinically asymptomatic or manifested variously range from undifferentiated fever, dengue fever, to severe and life-threatening forms of dengue hemorrhagic fever.^{6,7} Case definition of dengue hemorrhagic fever requires 4 diagnostic components: (1) acute fever lasting two to 7 days; (2) spontaneous hemorrhagic manifestations or a positive Tourniquet test; (3) thrombocytopenia ($\leq 100,000$ cells/mm³); and (4) evidence of plasma leakage.^{4,5,8} Dengue virus has 4 serotypes, i.e. DENV-1, DENV-2, DENV-3, DENV-4. All of which has a correlation with the severity of

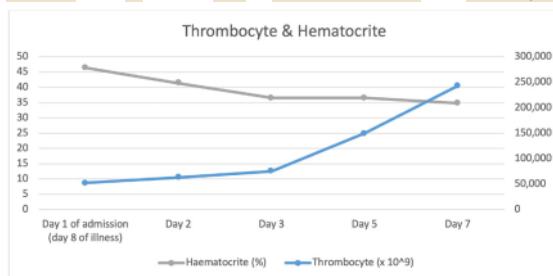


Figure 4. Funnel plot of studies investigating the prevention of tumor lysis syndrome

Table 1. Serum urea, creatinine and hemodialysis during admission

Day of admission	Urea (mg/dl)	Creatinine (mg/dl)	Treatment
Day 1	237 (pre)	19.49 (pre)	1 st hemodialysis
	149 (post)	12.54 (post)	
Day 3	172 (pre)	14.6 (pre)	2 nd hemodialysis
	82 (post)	9.12 (post)	
Day 5	148 (pre)	15.62 (pre)	3 rd hemodialysis
	91 (post)	7.4 (post)	
Day 7	113 (pre)	13.46 (pre)	4 th hemodialysis
	77 (post)	8.81 (post)	
Day 12 (discharged)	150	6.43	

dengue fever due to host immune response.¹⁵ A meta-analysis study by Soo, et. al. demonstrated that primary infection with DENV-3 from the Southeast Asia region, secondary infection with DENV-2, DENV-3, and DENV-4 from Southeast Asia region, and DENV-2, DENV-3 from non-Southeast Asia regions associated with severe dengue infections.^{9,10} In our case, the patient presented with fever, petechiae, thrombocytopenia, ascites; hence, fulfilled the criteria of dengue hemorrhagic fever. The fluctuating thrombocyte according to the day of illness, positive IgM serology supported dengue as the etiology in our case. Moreover, the patient contracted AKI. Dengue infection can affect many organs, including the kidney. Although not common, acute kidney injury complicates severe dengue infection in two to five percent of cases.¹¹ It is typically associated with hypotension and shock, as in dengue shock syndrome.^{11,12} Some factors that might be associated with AKI in dengue are male, older age, obesity, diabetes, coexisting bacterial infection.¹³ Interestingly, our young male patient had stable vital signs although he complained oliguria and laboratory exam showed proteinuria, increase in serum creatinine. Hypoperfusion due to shock was excluded as pre-renal etiology for AKI. The patient had no history of drug consumption which might injure the kidney. There was no sign of rhabdomyolysis or hemolysis. Other viral infection that may complicate the kidney such as hepatitis B, hepatitis C, had been ruled out. Renal injury in our case might be due to direct cytopathic effect of dengue virus, immune complexes deposition, or inflammatory response.^{2,11,14} Renal biopsy, unfortunately, was not performed. Primary dengue infection and dengue serotype played a role in this clinical manifestation. However, we did not do a dengue serotype examination. A cohort study by Porter et. al. in 2005 in Bandung, West Java detected all four serotypes with predominant of DENV-2.¹⁵ Yet, serotype shift might occur as reported in Indonesia dengue hemorrhagic fever epidemiology study by Harapan, et. al.⁵ The patient finally recovered, showing reversibility of the illness caused by dengue.

Conclusion

Dengue infection can manifest in various degrees of illness. AKI might happen in a hemodynamically stable dengue hemorrhagic patient. Although not usual, a direct cytopathic effect or inflammatory reaction might underlie renal injury in dengue. Appropriate treatment and close monitoring can result to a better outcome since the process is reversible.

Disclosure

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