

Dengue Fever-Induced Thrombotic Microangiopathy: An Unusual Cause of Renal Failure

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ABSTRACT

Dengue fever is a tropical infection caused by the dengue virus and spread by Aedes mosquitoes. About half of dengue infections are asymptomatic, and most present with fever and body ache. The complications are well known, including acute kidney injury (AKI). AKI in dengue is due to pre-renal cause. Thrombotic microangiopathy is a rare complication of dengue fever. This case is about dengue fever-induced thrombotic microangiopathy, giving accurate diagnosis and treatment.

Keywords: Kidney injury, Thrombotic microangiopathy, corticomedullary differentiation

INTRODUCTION

Dengue is an RNA virus belonging to the Flaviviridae family. Dengue patients have both typical and atypical presentations. Of these, acute kidney injury has been a rare manifestation. Mostly dengue with AKI occurs mainly due to dehydration and loss of fluids, leading to pre-renal failure. Thrombotic microangiopathy is an uncommon complication in dengue. Activation of the complement pathway is important in thrombotic microangiopathy (Upadhaya *et al.*, 2020). Classic and lectin pathways activate it. Infections can also trigger alternate pathway activation. Deposition of C3b on surface of pathogens with complement factor B forms alternative pathway i.e., C3b/Bb C3-convertase, which cleaves additional C3, resulting in the positive feedback mechanism. C3b is deposited on the surface of pathogens and binds to specific receptors on leukocytes, resulting in phagocytosis of complement-tagged cells. This article describes an atypical presentation of dengue fever manifesting as thrombotic microangiopathy (Gupta *et al.*, 2012).

Case Report

A 32-year-old male is presented with fever and body ache of 4 days. The patient was detected to be dengue-positive by non-structural protein 1 antigen testing. He was managed conservatively with intravenous fluids. Over the next few days, the patient's urine output gradually reduced, the patient was afebrile and dyspnoeic. He had pallor and generalized swelling all over the body. The patient had no history of kidney disease, diabetes mellitus, or hypertension. No history of drug intake. On Investigations: haemoglobin-9.3 g/dl, platelet count -76,000/cumm and serum creatinine-10.6 mg/dl. The peripheral blood smear shows the presence of schistocytes, spherocytosis, and polychromatophils. Reticulocyte count was 6.8%. Serum electrolyte levels were normal. Total serum protein 4.74 g/dl, and serum albumin 2.55 g/dl. Prothrombin time measured 13.5 s, with an INR of 1.3. Serum LDH level was 1349 mg/dl. Twenty-four hours urine output was 360 ml. Urine examination revealed proteinuria and microscopic haematuria. Urine spot PCR 1.48. C3 and C4 levels are normal. Serum ANA, cytoplasmic-ANCA, and perinuclear-ANCA was negative. USG kidneys showed normal-sized kidneys, with raised cortical echogenicity and partial loss of corticomedullary differentiation, suggesting Grade II medical renal disease. Because of reduced urine output, anaemia, and volume overload, haemodialysis was started with packed red blood cells.

Later kidney biopsy was taken. For light microscopy and immunofluorescence studies, two linear renal tissue was sent. Biopsy showed features of thrombotic microangiopathy with

glomerular capillary microthrombi along with the fibrillary appearance of mesangium. Few glomeruli showed solid bloodless appearance and focal reduplication of the glomerular capillary basement membrane. Proximal tubules showed focal flattening of lining epithelium, and interstitium showed mild lymphocytic infiltrate. Blood vessels showed mild intimal oedema. The patient was managed initially with haemodialysis for 2 days and fluid restriction. Gradually, over a period of 8 days, the patient's swelling and urine output improved. Investigations at discharge were haemoglobin level 10.5 g/dl, platelet count 403,000/cumm, serum creatinine 2.31 mg/dl, and LDH 266 mg/dl. Peripheral smear was normal—reticulocyte 0.8%. During follow-up, the patient was asymptomatic with normal renal function.

Discussion

Renal involvement identified in patients with dengue fever includes acute tubular necrosis, haemolytic uremic syndrome, and nephrotic syndrome. Shock secondary to dengue shock syndrome or haemorrhage, which leads to acute tubular necrosis, is the leading cause of AKI. AKI is important, uncommon manifestation of dengue (Khalil *et al.*, 2012). Thrombotic microangiopathy is a severe occlusive microvascular thrombotic syndrome that is characterized by profound thrombocytopenia, microangiopathic haemolytic anaemia, and symptoms of organ ischemia. ADAMTS13 inhibitor has been associated with dengue fever-thrombotic microangiopathy. In this case, the ADAMTS13 activity was <5% of the normal human plasma, and antibodies to ADAMTS13 were also detected. Most cases in the literature were treated with plasmapheresis and had full recovery on follow-up; however, in our case, the patient recovered without plasmapheresis. Hence, the role of plasmapheresis in such patients is debatable. Our case is important for its rarity and uncommon pathological picture. It is important to highlight such cases to understand the true prevalence of varying forms of AKI in patients suffering from dengue. It is important to diagnose these cases early to plan appropriate management and prevent life-threatening complications.

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Study significance: The prevalence of varying forms of AKI in patients suffering from dengue requires early diagnosis to plan appropriate management and prevent life-threatening complications.

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