Acute tubular necrosis in dengue fever in a child

Sir,

An 8 year old male child was brought with the complaints of fever for 5 days, vomiting, abdominal pain, and progressively increasing swelling of face, abdomen, and legs since 1 day. There was no history of hematuria, rashes, loose stools, or bleeding manifestations. An epidemic of dengue fever (DEN 2) was going on in the entire north India. On examination, blood pressure was 130/90 mm Hg (>95th centile), facial puffiness, bilateral pitting pedal edema, decreased breath sounds basal areas of the lungs, hepatomegaly (3 cm below right costal margin) and shifting dullness in the abdomen were present. His blood urea was 122 mg/dL and serum creatinine 4.3 mg/dL. Dengue serology (IgM and IgG) and NS-1 antigen tests were positive. Urinalysis showed full field red blood cells, +2 proteinuria, and no white blood cells. Ultrasonography of abdomen showed normal size kidneys with bilateral bright echotexture with accentuated corticomedullary differentiation and no obstruction. Rests of the investigations were normal.

The child was treated symptomatically and antihypertensive medications were started. Acute kidney injury persisted beyond 4 weeks; hence, a renal biopsy was performed. Light microscopy showed 15 glomeruli that appeared mildly enlarged with some showing mild increase in mesangial matrix and cellularity. The basement membrane appears unremarkable on silver methenamine stain. The tubules showed necrotic debris within lumina and focal vacuolization of lining epithelium. Small blood vessels and interstitium appear unremarkable. Tissue sent for immunofluorescence showed five glomeruli that were negative for all immunoglobulins and complements. Final diagnosis of mesangial proliferative glomerulonephritis and acute tubular necrosis was made [Figure 1]. Gradually renal function tests improved and blood pressure normalized. He was discharged on a serum creatinine of 0.9 mg/dL.

Acute kidney injury is a poorly studied complication of dengue infection in children. Proteinuria and abnormal urine sediment are the most common renal manifestations in patients with dengue fever. Several types of acute kidney injury in dengue infection has been reported that

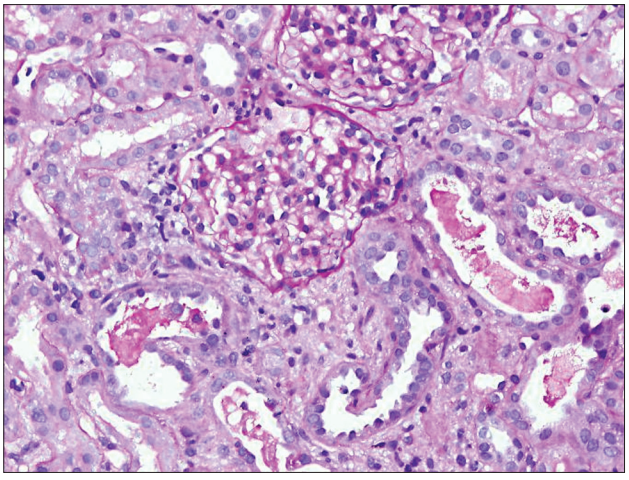

Figure 1: Microphotograph showing necrotic debris in tubular lumina (PAS, 200x)

include acute tubular necrosis, which may be associated with interstitial edema and mononuclear infiltration, acute glomerulonephritis, thrombotic microangiopathy, and myoglobinuric renal failure within the context of multiorgan failure.[1] The most common conditions associated with acute kidney injury are prolonged shock with metabolic acidosis, and severe DIC that lead to hypoxia/ischemia and result in multiple organ dysfunctions.[2]

The clinical picture in the index case was atypical in that the acute kidney injury was not associated with bleeding manifestations, shock, hemolysis, or rhabdomyolysis. This patient had acute tubular necrosis (ATN) and recovered spontaneously. Review of the literature revealed six cases of dengue fever with acute kidney injury without shock or bleeding manifestation. The cause of hematuria and proteinuria in our case appear to be mild proliferative glomerulonephritis. Though uncommon, hematuria, and proteinuria has been reported in ATN.[3] Histopathology in cases of the acute kidney injury due to dengue infection is scarce, and most of the diagnosis of acute tubular necrosis is made on clinical grounds.

The mechanism of renal involvement in children with dengue fever without bleeding or hypotension remains unclear. It has been postulated that dengue virus can cause direct invasion of the kidneys.[4] Jessie et al. investigated the cellular localization of dengue virus in naturally infected human tissue by applying immunohistochemistry and in situ hybridization techniques in tissue specimens obtained from serologically or virologically confirmed dengue infection. In the kidney viral antigens were detected as discrete granular deposits within the lining cells in the tubules.[5]

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