Collapsing glomerulopathy associated with hepatitis B infection: A case report

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ABSTRACT

Collapsing glomerulopathy has been classified as a variant of focal segmental glomerulosclerosis. It is associated with infections, inflammations, and certain medications. While its association with human immunodeficiency virus has been well established its occurrence with hepatitis B has not been reported. We present here a case of collapsing glomerulopathy in a child with hepatitis B infection.

Key words: Collapsing glomerulopathy, hepatitis B infection, lamivudine

Introduction

Collapsing glomerulopathy has been defined as the presence of segmental capillary tuft collapse in at least one glomerulus. Earlier it was considered to be a variant of focal segmental glomerulosclerosis, however a new classification has been proposed that further subdivides collapsing glomerulopathy into three subtypes based on the underlying etiology (idiopathic, genetic, or reactive).[1] Human immunodeficiency virus and parvovirus B19 are the most common infections implicated in the occurrence of infection induced collapsing glomerulopathy. We report here a 6-year-old child diagnosed with hepatitis B virus infection and collapsing glomerulopathy. This association has not been not been reported in literature.

Case Report

A 6-year-old boy presented with progressively increasing swelling over the body for 3 months, decreased urine output for 2 months; fever, cough, and respiratory distress for 6 days. There was no history of hematuria, dysuria, palpitations, chest pain, or jaundice. He had taken some treatment irregularly for these complaints, details of which were not known. On examination, he had severe respiratory distress due to pulmonary edema. His pulse rates were 155/min with all peripheral pulses well palpable; respiratory rates were 62/min with intercostal and subcostal recessions. He was anemic, hypertensive (blood pressure - 140/86, >99th centile) and had generalized anasarca and abdominal wall cellulitis. There was no jaundice, rash, arthritis, lymphadenopathy, or organomegaly. Systemic examination revealed bilateral basal crepts; there was tachycardia, but no murmur.

Investigations revealed anemia (hemoglobin [Hb] 6.3, microcytic hypochromic type), neutrophilic leukocytosis (total leukocyte count 14,800 with neutrophilia 87%) and renal dysfunction (blood urea 283 mg/dl, serum creatinine 3.9 mg/dl). The serum albumin levels were 1.6 gm/dl, cholesterol levels were 185 mg/dl and triglycerides of 472 mg/dl. The liver function tests were normal with a serum bilirubin

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of 0.3 mg/dl, alanine aminotransferase 14 IU/L and aspartate aminotransferase of 28 IU/L. The serum sodium levels were 143 mEq/L and potassium 5.9 mEq/L, total calcium 7.9 mg/dl, phosphates 3.6 mg/dl and SAP 181 IU/L. The venous blood gas showed mild acidosis (bicarbonate levels 16.7 mEq/L). The urine examination showed nephrotic range proteinuria with microscopic hematuria and 8–10 WBC/hpf. Radiology revealed pulmonary edema on chest radiograph and minimal pericardial effusion on echocardiography. A diagnosis of rapidly progressive glomerulonephritis with abdominal wall cellulitis was made, and the child started on intravenous antibiotics, furosemide and antihypertensives.

In view of worsening renal functions and hyperkalemia, hemodialysis was initiated. The child received two blood transfusions. Further investigations revealed that antinuclear antibody and anti-streptolysin-O-antibody were negative, complement levels (C3) were low and the serology was positive for hepatitis B (hepatitis B surface antigen, hepatitis B e antigen [HBeAg] and anti-hepatitis B core antibody [IgG anti HBc] positive; and anti-HBeAg negative; DNA titers for viral load could not be done due to nonavailability). The anti-hepatitis C virus and anti-human immunodeficiency virus (HIV) antibodies were negative. The renal biopsy showed features of collapsing glomerulopathy [Figure 1]. The light microscopy showed 18 glomeruli of which 10 showed glomerular capillary tuft collapse, three were segmentally sclerosed and five appeared unremarkable. The interstitium showed edema and a diffuse 30–40% of the tubulointerstitial compartment showed chronic parenchymal changes with blood vessels having mild medial sclerosis. Immunofluorescence showed nonspecific deposition of C3, IgM (2+), IgG, IgA. Hepatitis B antigen deposits were present in the glomerular tufts. Based on these findings and the serology report, a diagnosis of hepatitis B associated collapsing glomerulopathy was made. The child was started on lamivudine; was continued on diuretics and antihypertensives. After 2 weeks of antibiotic therapy the child improved and became dialysis independent. After 1 month of hospital stay the child was discharged on iron, calcium supplements, lamivudine and antihypertensives (amlodepine and furosemide). His blood urea and creatinine levels were 114 mg/dl and 1.9 mg/dl, respectively at discharge. At 6 months follow-up, the child was normotensive, with minimal edema and his kidney function test were urea of 86 mg/dl and creatinine 1.1 mg/dl. The serum albumin was still low (1.6 g/dl) and Hb had improved to 10 g/dl. Subsequently, the child has been lost to follow-up.

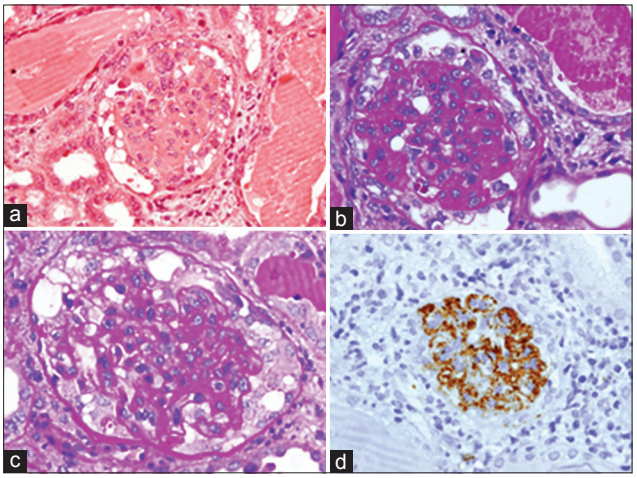

Figure 1: H and E (a) And PAS; (b) Stained microphotographs with collapse of glomerular tuft at ×200; (c) Collapse of glomeruli, prominence of visceral epithelial cells and protein reabsorption granules (PAS, ×400); (d) Hepatitis B antigen positivity in glomerular tuft (IHC, ×200)

Discussion

Collapsing glomerulopathy was first described in six subjects presenting with features of nephrotic syndrome and rapidly progressive renal failure and histological findings of collapse of glomerular capillary loops and significant tubulointerstitial damage.[2] It can occur secondary to viral infections like HIV, parvovirus B19, cytomegalovirus, campylobacter enteritis; in autoimmune diseases, guillaine barre syndrome, hematological malignancies and medications like bisphosphonates, interferon-alpha, and valproic acid. A significant proportion of collapsing nephropathy may be idiopathic.

Renal involvement is one of the most common extrahepatic manifestations of hepatitis B infection in children. Most children present with features of nephrotic syndrome. Immune-mediated mechanisms appear to be the predominant cause for the renal injury. The renal histology commonly reported with hepatitis B associated renal disease are membranous nephropathy, membranoproliferative glomerulonephritis, focal segmental glomerulosclerosis, and IgA nephropathy.[3] However collapsing nephropathy has not been reported with hepatitis B infection to best of our knowledge. Hepatitis B infection is rare in developed countries (due to universal hepatitis B immunization) and most reported cases are from Africa and Asia. Many countries of Asia and Africa have HBV prevalence of 8–15% and fall in the high endemic zone for the virus.[4] The transmission of the virus in endemic areas is primarily vertical from mother to child while horizontal modes contribute to transmission in moderate prevalence areas.

The natural history of hepatitis B associated nephropathy is not clear in children. Membranous nephropathy is most commonly associated with hepatitis B infection. While it resolves spontaneously or with antiviral agents in a majority in children, rarely it may progress to end-stage renal disease. Collapsing glomerulopathy in most patients due to any underlying cause is associated with poor prognosis. Our patient did respond to lamivudine initially but was lost to follow-up after 6 months. Treatment modality for hepatitis B mediated renal disease in children is primarily antiviral agents. Interferons are indicated if there is a concomitant liver injury. While lamivudine and entecavir can be is used in younger patients, other agents such as tenovir and adefovir are approved for use beyond 12 years. Telbivudine can be used in children above 16 years.[5-7]

To conclude, our patient had a collapsing glomerulopathy secondary to hepatitis B infection that partially improved on treatment with lamivudine. While membranous and membranoproliferative lesions are more common in hepatitis B mediated disease in pediatric age group, rarely collapsing glomerulpathy may also occur.

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Conflicts of interest

There are no conflicts of interest.

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