Case Report

Nephrotic proteinuria and renal involvement in HIV-infected children

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Abstract

HIV-associated nephropathy (HIVAN) has been reported in HIV-infected adults. HIVAN in children has not been described previously from the Indian subcontinent though we had reported earlier about non-nephrotic range proteinuria in HIV-infected children and their response to antiretroviral therapy (ART). We now report two children with HIV and nephrotic range proteinuria who demonstrated proliferative glomerulonephritis and mesangial hyperplasia, respectively.

Key words: Children, HIV nephropathy, HIV-associated nephropathy

INTRODUCTION

In 1984, physicians in New York and Miami reported HIV-infected adult patients with heavy proteinuria and rapid progression to end-stage renal disease. These patients showed large edematous kidneys with combination of focal segmental glomerulosclerosis (FSGS) and tubulointerstitial lesions. This renal syndrome, named HIV-associated nephropathy (HIVAN), was found predominantly in African Americans. Subsequent studies confirmed the presence of HIVAN in children in America and Africa, who frequently develop nephrotic syndrome in association with focal segmental glomerulosclerosis (FSGS) and/or mesangial hyperplasia with microcystic tubular dilatation.[1-3] HIVAN in children has not been described previously from the Indian subcontinent though we had reported earlier about non-nephrotic range proteinuria in HIV-infected children and their response to antiretroviral therapy (ART).[4] We now report two children with HIV and nephrotic range proteinuria who demonstrated proliferative glomerulonephritis and mesangial hyperplasia, respectively.

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CASE 1

A 14-year-old HIV-infected boy presented with recurrent diarrhea for past 12 years and recurrent respiratory infections for 3 years. He had received a blood transfusion 2 years ago. Both parents were also HIV infected. On examination, he had normal blood pressure, weight of 25 kg, height of 132 cm, clubbing, and cervical lymphadenopathy. The other physical examination was normal. Investigations showed hemoglobin of 10.5 gm/dl, WBC count of 8,900/cumm [68% polymorphs, 30% lymphocytes], ESR of 105 mm at end of 1 hour, SGPT of 68 IU/L, Blood urea nitrogen (BUN) of 13 mg/dl and serum creatinine of 1.6 mg/dl. The other serum chemistries were within normal limit. Mantoux test was 6 mm. Chest X-Ray was normal. Urine examination showed 1+ albuminuria with urine albumin/creatinine of 2.6 and 24 hours urine albumin of 1188 mg/24 hours. Abdominal ultrasonography showed right kidney of 9.6 cm×4.6 cm and left kidney of 11.1 cm×3.9 cm. A kidney biopsy was done that showed 8 glomeruli

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with variable proliferation, irregular thickening of basement membrane, mesangial cell proliferation and one crescent with one sclerosed glomerulus suggestive of proliferative glomerulonephritis. His CD4 count was 115 cells/cumm (11%) with CD4:CD8 ratio of 0.13. Enalapril was started for proteinuria as well as bicarbonate supplements and antiretroviral therapy (ART) consisting of Zidovudine, Lamivudine, and Nevirapine. However, he was lost to follow-up subsequently.

CASE 2

A 7-year-old HIV-infected girl presented with jaundice, abdominal pain and clay coloured stools for 2 months. She was diagnosed to be HIV infected 6 months ago by two positive ELISA tests. Her mother was also HIV infected. Other two older siblings were HIV negative. The child had recurrent fever, diarrhea, and bilateral purulent otorrhoea for the past 1 year. She had received antituberculous therapy (ATT) when she was 6 ½ year old and she stopped it after 3 months of treatment. There was no history of blood transfusion. On examination, she had icterus, generalized lymphadenopathy, papular dermatitis and hepatosplenomegaly with bilateral crepitations over both lungs. Blood pressure was 100/70 mm of Hg and there was no edema. Investigations showed hemoglobin of 10.9 gm/dl, WBC count of 19,000/cumm [72% polymorphs, 22% lymphocytes], and platelet count of 2,37,000/cumm. The laboratory findings were as the followings; total bilirubin 7.3 mg/dl with direct bilirubin 6.1 mg/dl, SGOT 125 IU/L, SGPT 57 IU/L, GGTP 56 IU/L, serum alkaline phosphatase 1025 IU/L, total proteins 7.3 gm/dl, albumin 1.7 gm/dl, prothrombin time 18 seconds, and partial thromboplastin time (PTT) 31 seconds. She had hypokalemia (potassium=2.6 mEq/L) with sodium of 134 mEq/L. Ultrasound of abdomen showed hepatosplenomegaly with medical renal disease. Urine examination showed presence of bile salts and bile pigments with 2+ proteinuria. Urine albumin/creatinine was 6.6 and 24 hours urine albumin was 47 mg/kg/day. Serum creatinine was 0.6 mg/dl. Hepatitis virus profiles including HBsAg, anti-hepatitis A and anti-HCV ELISA were negative. Chest X-Ray showed bilateral lower zone infiltrates. Serum ceruloplasmin was normal. Antinuclear antibody and double stranded DNA (dsDNA) were negative. There was no Krayer-Fisher KF ring on slit lamp examination. CD_4 cell count was 221 cells/cumm (8.16%) with CD_4:CD_8 of 0.1. She was treated with intravenous antibiotics for the pneumonia but there was no response. She was then started on three drug ATT consisting of ciprofloxacin, ethambutol, and streptomycin in view of tuberculosis defaulter status, liver dysfunction, and non-improving pneumonia. Her bilirubin normalized after 1 month but liver enzymes were still elevated (SGOT=185 IU/L, SGPT=110 IU/L). She was started on enalapril for her proteinuria and underwent a renal biopsy after the jaundice resolved. Light microscopy showed 16 glomeruli with mesangial matrix widening, thin glomerular basement membrane with focal interstitial inflammation, and marginal increase in mesangial cells. On enalapril, her serum albumin increased to 3.7 gm/dl after 3 months of therapy and proteinuria decreased to trace. After 6 months of ATT, she was started on combined ART consisting of zidovudine (AZT), lamivudine (3TC), and nevirapine (NVP).

DISCUSSION

HIVAN is now the third leading cause of end-stage renal disease (ESRD) in African Americans between the ages of 20 and 64 years. Statistics in the United States estimate the incidence of HIVAN to be between 3.5–12%.[5] Patients usually present with advanced HIV infection, renal insufficiency, and marked proteinuria.[6] In both our patients, there was advanced HIV disease with nephrotic range proteinuria though renal insufficiency was as yet not present. Kidneys are usually enlarged and show hyperechogenecity on abdominal ultrasound.[3] Our patients' ultrasound for the kidneys showed normal sizes though there was increased echogenecity in the 7-year-old girl. Histopathology of HIVAN is characterized by focal segmental glomerulosclerosis and/or mesangial hyperplasia with microcystic tubular dilatation. Histopathology was suggestive of mesangial hyperplasia in both patients though tubular changes were not seen.

The pathogenesis of HIVAN is not exactly established though viral infection of renal cells have been postulated to play a key role in the pathogenesis of HIVAN by partially affecting the growth and differentiation of glomerular and tubular epithelial cells and enhancing the renal recruitment of infiltrating mononuclear cells and cytokines. These changes enhance the infectivity of HIV-1 in the kidney and induce injury and proliferation of intrinsic renal cells.[1] Low CD_4 count is associated with subsequent development of chronic renal disease.[7] In both our patients CD_4 counts were low (the boy had a low CD_4 percent) but they had not progressed to chronic renal failure as yet.

Highly active antiretroviral therapy (HAART) is effective in preventing ESRD and angiotensin converting enzyme (ACE) inhibitors also have a role.[6,7] In our report, the HIV infected girl had

diminished proteinuria on ACE inhibitor, whereas the boy was lost to follow-up and hence response to therapy could not be assessed.

In conclusion, this is a first report of nephropathy in HIV-infected children leading to nephrotic range proteinuria in Indian children with advanced disease. Regular screening with renal function tests, blood pressure and urine examination is useful for detecting renal disease early and prevent progression to HIVAN.

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