Case Report

Remission of HBV-related mesangioproliferative glomerulonephritis after interferon therapy

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Introduction

Glomerulonephritis is an uncommon but well-described complication of chronic hepatitis B virus (HBV) infection [1]. Corticosteroids and other immunosuppressive drugs are of no benefit [2], and may actually increase the morbidity and mortality [3]. Interferon (IFN) therapy has been used in small numbers of patients with HBV-associated membranous and membranoproliferative glomerulonephritis [4]. We report here a case of mesangioproliferative glomerulonephritis and chronic hepatitis due to HBV infection, who benefited from IFN therapy.

Case

A 23-year-old unmarried male developed jaundice preceded by a typical prodrome in September 1995. Jaundice persisted for 3 weeks and resolved spontaneously. Hepatitis B surface antigen (HBsAg) was found to be positive, but the source of infection could not be identified. In the last week of December 1995 he noticed facial puffiness followed by swelling of the whole body. He had proteinuria of 2.1 g/day and had been taking diuretics with which oedema subsided. In March 1996 he again developed swelling of the whole body and was admitted at our Institute.

There was no family history of jaundice, blood transfusions, or infections in the past. There were no other apparent causes of HBV infection. The patient was a social drinker. Physical examination revealed pedal oedema but no icterus, facial puffiness, or lymphadenopathy. His blood pressure was 120/86 mmHg. There were no stigmata of chronic liver disease. Liver was palpable 2 cm below right costal margin (span 12 cm). There was no splenomegaly or free fluid in the abdomen. Systemic examination revealed no other abnormality.

Investigation at admission revealed a haemoglobin of 10.6 g/dl with normal total and differential leucocyte and platelet counts, serum bilirubin 0.6 mg/dl, aspartate aminotransferase (AST) 73 IU/l (normal 2–20), alanine aminotransferase (ALT) 85 IU/l (Normal 2–15), alkaline phosphatase 160 IU/l (normal 70–140), albumin 2.6 g/dl, globulin 3.7 g/dl, and creatinine 1 mg/dl. Urine examination revealed 3+ proteinuria and 24-h urinary protein was 2.0 g. HBsAg and hepatitis B e antigen (HBeAg) were positive after 6 months of illness. There was no evidence of cirrhosis on ultrasound examination of the abdomen. Light microscopy of renal biopsy tissue revealed mesangioproliferative glomerulonephritis. Immunofluorescence showed 2+ deposition of immunoglobulin (Ig) G and M and complement 3 (C3) in the mesangium and along the capillary loops. There was no deposition of IgA. Liver biopsy, carried out after 6 months of illness, showed chronic hepatitis with moderate severity of necro-inflammatory activity. Immunostaining for hepatitis B core antigen (HBcAg) was positive. A diagnosis of chronic hepatitis B with mesangioproliferative glomerulonephritis due to replicative HBV infection was made.

The patient was treated with interferon α-2b (Intron A, Schering Corp., Kenilworth, NJ), 3 MU subcutaneously daily for 16 weeks. In the first week of therapy he developed mild fever, nasal stuffiness, and myalgia which were treated symptomatically, and subsequently he tolerated interferon very well. Serial liver function tests showed significant fall in AST and ALT after 3 months and they became normal (Figure 1). Proteinuria also gradually decreased and became nil at the end of therapy. His serum albumin levels also increased and became normal. He seroconverted and became HBeAg negative and anti-HBe positive at the end of the therapy. Symptomatically he was feeling better. His transaminases continued to be normal and proteinuria was nil 12 months after stoppage of interferon.

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Remission of HBV-related MPGN after interferon

HBeAg and glomerulonephritis can be proved only by demonstrating disappearance of the glomerular abnormalities on histology with eradication of the virus. This is not easily done, for ethical reasons. However, clinical improvement of renal function abnormalities following seroconversion of virus either spontaneously or following interferon therapy as seen in our patient can be of use in proving this relationship.

The natural history of HBV-related glomerulonephritis is now well characterized [4–7]. Seroconversion to anti-HBe is associated with remission of proteinuria. Spontaneous remissions are common in children, these are rare in adults, but are more frequent with IFN therapy [2,6,7]. Our patient had replicative HBV infection and proteinuria; the clearance of HBeAg and remission in the proteinuria that occurred following interferon therapy suggests the role of IFN in the seroconversion as well as in the remission of proteinuria. However, the remote possibility of a spontaneous remission cannot be totally excluded. The response to IFN therapy found in patients with glomerulonephritis is higher than seen in patients with chronic hepatitis B [4]. Conjeevaram et al. [4] have reported a small series of 15 patients with chronic hepatitis B and glomerulonephritis (membranous 10, and membranoproliferative 5) treated with IFN, and have shown a long-term serological response with sustained loss of HBeAg and HBV DNA in eight (53%) patients. Seven of eight responders have also shown a gradual but marked improvement in proteinuria. Lin [7] has reported the effect of IFN treatment in 40 children with HBV membranous nephropathy who failed to respond to corticosteroid treatment. All 20 patients who received IFN were free of proteinuria after 1 year of follow-up. Fifty per cent of the cases showed HBV seroconversion. However, in no treatment group, only seven (35%) were free of proteinuria and none showed HBV seroconversion.

Cases treated with IFN reported so far have had either membranous or mesangiocapillary glomerulonephritis [4]. Response is better in membranous as compared to mesangiocapillary glomerulonephritis [4]. In a recent study on the therapeutic effects of IFN on HBV-associated glomerulonephritis, two patients with mesangiproliferative glomerulonephritis were also included [8]. Both patients in this study showed remission of proteinuria with or without seroconversion to anti-HBe [8].

Our patient had mesangiproliferative glomerulonephritis and had remission of proteinuria along with seroconversion following IFN therapy. We therefore believe that mesangiproliferative glomerulonephritis in our patient was associated with HBV infection and it responded to interferon therapy.

We conclude that mesangiproliferative glomerulonephritis can be associated with chronic HBV infection and responds well to therapy with IFN.

Discussion

This case suggests the association of mesangiproliferative glomerulonephritis with chronic hepatitis due to replicative HBV. Proteinuria subsided with seroconversion to anti-HBe and loss of HBeAg after adequate interferon therapy, suggesting the pathogenetic role of HBV in producing mesangiproliferative glomerulonephritis and role of interferon therapy in this situation.

Several histological findings have been reported in renal biopsies obtained from patients with glomerulonephritis associated with chronic HBV infection; these include, membranous, membranoproliferative, mesangiocapillary, and mesangiproliferative glomerulonephritis, and focal glomerulosclerosis [1,2]. The pathogenesis of hepatitis B glomerulonephritis remains unknown. All the major hepatitis B virus antigens, including HBsAg, HBeAg, and HBeAg, have been located in the glomerular capillary wall or in the mesangium. This could be a result of non-specific passive trapping of immune complexes containing HBV antigens and may not be responsible for glomerular lesion, or this may be due to local immune-complex formation at these sites [5].

The cause and effect relationship of HBV infection and glomerulonephritis can be proved only by demonstrating disappearance of the glomerular abnormalities on histology with eradication of the virus. This is not easily done, for ethical reasons. However, clinical improvement of renal function abnormalities following seroconversion of virus either spontaneously or following interferon therapy as seen in our patient can be of use in proving this relationship.

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References


Received for publication: 8.1.98

Accepted in revised form: 9.9.98