Hepatitis C as a potential cause of IgA nephropathy

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ABSTRACT

This is a case report of a 16-year-old boy presenting with a history of oliguria and anasarca. Workup revealed marked proteinuria to the tune of 8 g/day. He was subsequently found to be hepatitis C positive. Genotype was hepatitis C virus type 6. Renal biopsy revealed mesangioproliferative glomerulonephritis with IgA deposits consistent with IgA nephropathy (IgAN). Initiation of oral ribavirin and pegylated interferon caused a marked reduction in proteinuria after 8 weeks of treatment. It was postulated that hepatitis C manifested as IgAN. This case report thus sheds light on the possibility of an association between hepatitis C and IgAN.

Key words: Hepatitis C, IgA nephropathy, renal biopsy

Introduction

Renal disease associated with hepatitis C virus (HCV) infection includes membranoproliferative glomerulonephritis commonly with or without cryoglobulinemia, and membranous glomerulopathy.[1] But there are a few case reports of IgA nephropathy (IgAN) related to hepatitis C. We report a patient with hepatitis C who was diagnosed as having IgAN. A causal association was surmised from the marked improvement with interferon (IFN) therapy.

Case Report

A 16-year-old boy presented with oliguria and gradually developing anasarca of 5 months duration. He did not have any symptoms to suggest a connective tissue disorder. He gave no history of frank hematuria or febrile illness prior to the onset of renal symptoms. He denied any history of prior blood transfusions or drug intake.

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On physical examination, he appeared relatively well with blood pressure (BP) 130/90 mm Hg and dependent pitting edema. Systemic examination was unremarkable.

Laboratory findings included hemoglobin of 12.7 g/dl and white blood cell (WBC) count of 4700 with normal differential. Peripheral smear showed normocytic, normochromic anemia. Serum creatinine and blood urea were 0.66 and 15 mg/dl, respectively. Serum triglyceride level was 234 mg/dl and cholesterol level was 330 mg/dl. Serum sodium and potassium were 145 and 4.33 mmol/l, respectively. His liver function test revealed a bilirubin of 0.13 mg/dl, AST of 43 mg/dl, ALT of 61 mg/dl, ALP of 150 mg/dl, with a total protein of 3.7 mg/dl and albumin of 1.2 mg/dl. Urine analysis showed 3+ proteinuria with occasional WBC and no red blood cell (RBC). Subsequently, a 24-h urine examination revealed a proteinuria of 8 g/day. Immunologic tests including cryoglobulins, ANA, dsDNA, and ANCA were negative, and complement levels were normal. Ultrasonography of the whole abdomen showed normal sized kidney, which were mildly echogenic.

Serologic testing revealed him to be hepatitis C positive. On further investigations, HCV-RNA PCR showed 2,478,600 copies. Genotyping showed it to be HCV type 6. Liver biopsy did not show any specific changes. No varices were present on upper gastrointestinal endoscopy.

Subsequently, the patient underwent renal biopsy with immunofluorescence staining, which revealed mesangioproliferative glomerulonephritis with IgA deposits consistent with IgAN.

He was subsequently started on oral ribavirin 200 mg twice daily and pegylated IFN 80 mcgm subcutaneously once a week for a period of 6 months. He improved symptomatically. After 4 weeks of anti-HCV therapy, a dramatic decrease in the 24-h urine protein excretion was observed from the initial 5.2 g/day to 238 mg/day. This response was even better after 8 weeks of therapy and the proteinuria decreased to 39 mg/day. No evidence of drug-related side effects was documented during this period. He is now on regular follow-up with us and is compliant with his medication.

Discussion

HCV has been associated with multiple extrahepatic manifestations, including cryoglobulinemia, glomerulonephritis, skin disorders (porphyria cutanea tarda and lichen planus), arthritis, a sicca-like syndrome, Mooren's corneal ulcer, and lymphoproliferative disorders. It has been shown that in humans, the principal renal manifestation of chronic hepatitis C infection is development of membranoproliferative glomerulonephritis (MPGN), most often associated with cryoglobulinemia.[1] Indeed, it is now regarded that HCV infection is the pathogenetic basis for the great majority of cases that were previously thought to be idiopathic MPGN and essential mixed cryoglobulinemia.[2,3] The renal manifestations are usually associated with long-standing (i.e., a greater than 10-year history) HCV infection. Most often there are concurrent clinical and laboratory features of chronic active hepatitis and/or cirrhosis. HCV glomerular disease has been most frequently identified in men; this disease process is rare in children. Although the percentage of HCV-infected patients with such manifestations is small, the problem is significant as the population at risk is so large.

Meanwhile, IgAN is the most common pattern of glomerulonephritis identified in all parts of the world where renal biopsy is widely practiced. The initiating event in the pathogenesis of IgAN is the mesangial deposition of IgA, which is predominantly polymeric IgA of the IgA1 subclass (pIgA1). With or without the additional deposition of IgG and C3, this could be associated with glomerular inflammation and injury, with the potential for that injury being either to resolve or heal with sclerosis. Co-deposits of IgG and complement components are not mandatory for disease activity or progression, and their presence at diagnosis does not correlate with clinical outcome. Subsequently, tubular atrophy and interstitial fibrosis could follow, leading to progressive renal failure. However, nephrotic-range proteinuria is uncommon, occurring in only 5% of patients with IgAN, and is more commonly seen in children and adolescents.

There have been isolated case reports of IgAN-complicated hepatitis C wherein improvement of the urinary protein was observed during IFN treatment.[4] With IFN treatment for nephropathy, decrease in the urinary protein and improvement of the urine sediment findings were observed. Action mechanisms of IFN for nephropathy were estimated. Although, persistent infections of HCV were observed in those cases, HCV-RNA was not identified and the urinary findings were improved by the IFN treatment.

There have also been case reports suggesting the presence of immunoglobulin A class antibody to HSV core antigen (IgA anti-HCc).[5] It was concluded that IgA anti-HCc is a useful marker to identify the presence of active type C liver disease and that the disappearance of IgA anti-HCc 3 months after IFN therapy predicts a good response in treated patients.

Thus, IgAN with hepatitis C is rare. Immune complex deposition as an extrahepatic manifestation of hepatitis C is well-known.[6,7] However, in these instances, MPGN has been the most common type. There have been isolated case reports of hepatitis C with IgAN.[8] Caution regarding the use of IFN and ribavirin has also been warranted in isolated studies worldwide.[9] The optimal dosing and its duration with follow-up are still not certain.

Moreover, demographically, hepatitis C genotype 6 with IgAN has not been reported from India. In addition, a dramatic improvement in proteinuria with anti-HCV therapy, as in our case, has not been documented to our knowledge in IgAN. Hepatitis C type 6 is most commonly encountered in Hong Kong. Presence of this genotype in India warrants a change in the understanding of the distribution of hepatitis C globally as well.

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