How Do We Treat Patients with Hepatitis C Virus Associated-glomerulonephritis?

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It is well known that extrahepatic manifestations often occur in hepatitis C virus (HCV) infection. Johnson et al first described 8 patients with membranoproliferative glomerulonephritis (MPGN) and HCV infection (1). Most of the cases showed nephrotic syndrome, hypocomplementemia, serum IgM rheumatoid factor and cryoglobulinemia. Although the mechanism by which HCV induces MPGN has not been known, cryoglobulin containing HCV, anti-HCV antibody and IgM rheumatoid factor may play an important role as an immune complex.

The question is how to treat this disease. Interferon alpha has been approved for treatment of chronic HCV infection. Interferon alpha may also induce renal injury (7).

Another therapeutic strategy is to manipulate the immune mechanisms by using corticosteroids, immunosuppressive agents and plasmapheresis. In a randomized controlled study, Dammarco et al (8) compared the treatment outcome among patients treated with either interferon alpha or prednisolone alone, or in combination. While a complete response was achieved in 8 of 15 (53.3%) patients treated with interferon alpha and in 9 of 17 (52.9%) treated with interferon alpha plus prednisolone, it was found in only 3 of 18 (16.7%) patients who received prednisolone only and in 1 of 15 (6.7%) untreated controls. In the 3 patients in the prednisolone group, improvement of clinical manifestations was observed without significant changes in HCV RNA levels. In contrast, in 5 of 13 (38.5%) HCV RNA-positive non-responsive patients, a significant increment of HCV RNA levels was demonstrated. Quigg et al reported a case of membranoproliferative glomerulonephritis with cryoglobulinemia and HCV infection (9). In that case cyclophosphamide was very effective and within 1 month of initiating therapy, the patient’s cryoglobulin became undetectable in serum. After 3 months the patient’s renal function became normal, although serum levels of HCV RNA increased.

Komatsuda et al reported the effectiveness and safety of corticosteroids in HCV-associated nephropathy (10). They treated 16 patients with various types of glomerulonephritis and HCV infection with interferon alpha or corticosteroids. Five patients were treated with interferon alpha without a remarkable effect on renal impairment, whereas 5 of 11 patients treated with steroids showed a decrease in the serum creatinine level and urinary protein excretion. However, after the cessation of interferon therapy, all of those who had responded to the therapy showed recurrence. Johnson et al also reported the efficacy of interferon alpha in HCV-associated glomerulonephritis (3). Fourteen patients received interferon alpha at the dose of 3 million units thrice weekly for 6–12 months with a significant reduction in proteinuria but no improvement in renal function. A good clinical response was correlated with disappearance of HCV RNA from serum during the treatment. However, relapse of viremia and renal disease was common after completing the therapy. Since then many reports including the effect of high-dose interferon (4), ribavirin (5), which is a nucleoside analogue with activity against viruses, and a combination with interferon and ribavirin (6) have been published, and the results were inconsistent. The side effects of interferon alpha are dose dependent and are more frequent with increased duration of therapy. Interferon alpha may also induce renal injury (7). Thus, the optimal dose and duration of interferon therapy in HCV-associated glomerulonephritis have not been established.

Immunosuppressive therapy may be useful to treat patients who do not show a favorable result or can not tolerate interferon, although it is not certain that immunosuppressive therapy ameliorates the long-term prognosis of this disease.
References


