Glomerular Diseases

Treatment of Hepatitis Related Glomerulonephritis

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Introduction: Hepatitis associated glomerulonephritis (GN) is an extrahepatic syndrome caused by chronic viral hepatitis, and this injury is medicated by immune complexes. Hepatitis B virus (HBV) and hepatitis C virus (HCV) can cause glomerular lesions such as membranous glomerulonephritis (MGN), membranoproliferative glomerulonephritis (MPGN), and IgA nephropathy. MGN is most common disease caused by HBV infection otherwise MPGN is commonly caused by HCV infection. Clearance of viral antigens with antiviral agents results in improvement of proteinuria, but effects of immunusuppressive agents remain unproven.

Treatment of HCV related GN: Chronic HCV infection is about 10% of chronic hepatitis in Korea, while HBV is more than 70% of all chronic hepatitis. The most common renal involvement of HCV infection is essential mixed cryoglobulinemia leading to type I MPGN, or MPGN without cryoglobulinemia, MGN. Recent standard treatment of HCV is pegylated interferon alfa (Peg-IFN α) with ribavirin, and rate of sustained viral response (SVR) is increased 80-90% (genotype 2 or 3). Risk of GN in patients with HCV is still unknown, clinical course of kidney disease is closely related with responses of HCV treatment.

Standard antiviral treatment with peg-IFN α and ribavirin is recommended, but ribavirin should be used with extreme caution to the patients with GFR <50%. In cases of severe pathologic inflammation, nephrotic range proteinuria and/or rapid decline of renal function, intravenous methylprednisolone pulse therapy (0.5-1.0 g) followed by oral prednisone (0.5 mg/kg) and cyclophosphamide (1-2 mg/kg) can be used.

In cases of mixed cryoglobulinemia (MC), plasmapheresis could be helpful for removal of cytokines, immune complexes, but immunosuppression should be along with pheresis. Rituximab has been given encouraging results in HCV with MC, randomized trials are warranted to clarify risk to benefit ratio.

Treatment of HBV related GN: HBV induced renal tissue injuries could be caused by cytotoxic effect of virus, immune complex mediated, HBV induced immune reaction, or indirect cytokine effect. Clinical presentations in adults are commonly nephrotic syndrome, and pathologic findings usually show MGN and often show combination with IgA nephropathy. Different from children, spontaneous remission is rare and >50% of nephrotic patients with abnormal liver function can progress to ESRD within 3 years.

Antiviral treatment is most important in managing HBV related GN. Entecavir, tenofovir, or Peg-IFN α is recommended to HBeAg (+) patient with HBV DNA ≥20,000 IU/mL (≥2,000 in HBeAg (-) or cirrhosis), doubling of AST/ALT level or liver biopsy proven hepatitis. There is lack of randomized controlled trial between antiviral treatment and combination with immunosuppressive agents for treatment of HBV associated GN. Although immunosuppressive agents can increase HBV replication, corticosteroid had been tried for symptomatic relief of proteinuria, but it does not seem to have an ameliorative effect on nephrotic syndrome. Cytotoxic agents, with or without plasma exchange, can be used for the patient with polyartertitis nodosa or ANCA associated vasculitis due to HBV infection. Mycophenolate mofetil (MMF) and low dose steroid combined with antiviral agents showed partial remissions without significant viral replication.

Conclusion: There is still no proven clinical guideline for the treatment of hepatitis related GN except for antiviral treatment. Proliferative, progressive kidney disease can be managed by careful steroid and immunosuppressive agents, but optimal antiviral therapy must be combined. After development of recent anti viral agents, treatment resistant strains have diminished and clinical outcomes have improved. Decrement of viral activity seems to improve renal manifestation of hepatitis and to improve renal survival. Effectiveness of combined immunosuppression in hepatitis related GN need to be defined by well-designed randomized controlled studies.