Dear Sir,

End-stage liver disease is frequently complicated by a variety of functional renal abnormalities, such as the hepatorenal syndrome and disturbances in salt and water metabolism. Morphological and functional glomerular changes also occur in liver disease. Concomitant hepatic and glomerular disease has been associated with viral hepatitis, various infectious diseases, vasculitis, lupus erythematosus, α-antitrypsin deficiency, biliary atresia, familial cirrhosis, Alagille syndrome, tyrosinemia, and cryoglobulinemia [1-3]. Cirrhosis has been associated with a glomerular lesion that in most cases reveals deposits of IgA and smaller amounts of other immunoglobulins and C3 in the mesangium [1]. We would like to present a patient with Wilson cirrhosis associated with membranoproliferative glomerulonephritis (MPGN).

A 13-year-old male patient was born to nonconsanguineous parents. He was first admitted to our center with complaints of edema and hematuria. Physical examination revealed 2+ pitting edema and ascites. His blood pressure was normal. Urinalysis showed 3+ protein with 30-35 red blood cells. His hemoglobin was 11.5 g/dl, erythrocyte sedimentation rate 22 mm/h. His serum creatinine was 0.6 mg/dl, AST 159 U/l, ALT 68 U/l, alkaline phosphatase 154 U/l, total protein 5 g/dl (albumin 2.6 g/dl and globulin 3.4 g/dl), phosphorus 2.8 mg/dl, total bilirubin 1.8 mg/dl and conjugated bilirubin 0.7 mg/dl. The serum was negative for both hepatitis B surface antigen and antibody against hepatitis C virus. Serum immunoglobulins were high: IgG 4,170 mg/dl, IgA 1,940 mg/dl, IgM 380 mg/dl. The serum complement C3 was 27.5 mg/dl, prothrombin time (PT) 35 s, partial thromboplastin time (PTT) over 1 min. His abdominal ultrasonography revealed a normal sized liver with an increased echogenicity. Although liver and renal biopsies were planned, they were not carried out because of prolonged PT and PTT values in spite of repeated plasma transfusions. The patient was discharged and advised to attend follow-up visits.

Four months later, the patient was readmitted to our clinic with high fever and gross hematuria. From his history, it was understood that he was diagnosed with Wilson cirrhosis at another hospital. The diagnosis was established by the appearance of corneal Kayser-Fleischer rings and a high rate of urinary copper excretion and macro/micronodular cirrhosis.
in the liver biopsy. On admission, his abdominal ultrasonography revealed a slightly enlarged liver with a diffuse increase in echogenicity. The spleen was also enlarged, and a moderate amount of ascitic fluid, and minimal pleural effusions were detected. Laboratory evaluation revealed the following: serum cryoglobulins were negative, antibody to smooth muscle antibody weakly positive (1/20), α1-antitrypsin 130 mg/dl (80-200 mg/dl), ceruloplasmin 3.0 µg/dl (20-54 µg/dl). The urinary copper excretion rate was 1,210 µg/24 h. A percutaneous renal biopsy showed mesangial proliferation, moderate thickening of the glomerular basal membrane and an increase of the lobulation in some glomeruli. Immunofluorescence studies showed a mesangial staining for IgA (3+), IgM (1+) and IgG (1+). Hepatic glomerulonephritis secondary to Wilson cirrhosis was established by these physical and laboratory findings. Z-Penicillamine and zinc therapy were started and the patient was transferred to a transplantation center for liver transplantation.

Liver disease may play a role in the development of glomerulonephritis [3]. Several types of glomerulonephritis, including membranous glomerulonephritis and MPGN, have been documented in renal biopsies of children with end-stage liver diseases who had no prior history of renal disease [3, 4]. More clinical and immunopathological data suggest that glomerular deposition of circulating immune complexes is a major cause of the described morphological and functional changes. These patients reveal high serum IgA levels and renal IgA deposits [5]. It is suggested that IgA immune complexes formed against infectious and/or dietary antigens bypassing hepatic clearance may cause mesangial IgA deposits [6, 7]. The liver is believed to clear immune complexes from the circulation via its Kupffer cells. Accordingly, a diseased liver might be unable to clear these complexes, increase their circulating levels and cause increased trapping and deposition within the kidney [4].

Thus, it is possible that Wilson cirrhosis may also have played a role in the development of our patient’s MPGN.

The present patient is the second reported patient who developed MPGN secondary to Wilson’s disease according to our knowledge. Sarles et al. [8] have reported a patient with Wilson’s disease, IgA glomerulonephritis and vascular purpura. The IgA nephropathy and elevated serum IgA levels are probably due to the liver disease; clinical and histological manifestations of the renal disease may return to normal after liver transplantation.

References


Nephron 1996;74:497-498
Gündüz/Dünsel/Anarat