Membranoproliferative Glomerulonephritis in a Child with Liver Cirrhosis

K.	Kazunari	Kaneko
Y.	Yoshiharu	Suzuki
H.	Haruko	Watanabe
Y.	Yutaka	Fukuda
K.	Keiji	Yabuta

Department of Pediatrics, Juntendo University School of Medicine, Tokyo, Japan

Kazunari Kaneko, MD, Department of Pediatrics, Juntendo University School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113 (Japan)

Dear Sir,

Recently it has been focused that glomerulonephritis with end-stage liver disease (ESLD), which has been termed hepatic glomerulonephritis (HGN), occurs not only in adults, but also in children [1-3]. In terms of renal histology, although Milner et al. [1] have reported that membranoproliferative glomerulonephritis (mesangiocapillary glomerulonephritis; MCGN) is a common finding, Noble-Jamieson et al. [2] and Ohtomo et al. [3] have reported that mesangial proliferative glomerulonephritis with the mesangial deposition of IgA is a predominant histological finding in children with ESLD. Little is known about HGN in terms of prognosis and responsiveness to drug therapy such as prednisone. We wish to report on a young girl with MCGN caused by ESLD who seemed to respond to a short course of prednisone.

A 9-year-old girl suffering from ESLD by biliary atresia was recently referred to us by the pediatric surgeon because of the appearance of massive proteinuria and hematuria during follow-up for her impaired liver function. At the time of referral, her liver function was disturbed by cholestasis. The liver biopsy specimen revealed marked fibrosis. Urinalysis demonstrated nephrotic-range proteinuria (4.8-24.0 g/day) and hematuria (+++ by dipstick test) with a few red blood cell casts. Although her renal function was not disturbed (creatinine clearance 111 ml/min/1.73 m²), hypoproteinemia (total protein 46 g/l, normal 64-81; serum albumin 23 g/l, normal 40-53) and hypocomplementemia (C3 670 mg/l, normal 700-1,300; C4 180 mg/l, normal 200-500) were noted. The serum IgA level was slightly elevated (2,850 mg/l, normal 330-2,360), while the levels of serum IgG and IgM were not increased (9.5 g/l and

Fig. 1. a Light microscopic findings showing mesangial cell proliferation associated with capillary wall thickening. Periodic acid-methenamine. $\times 200$. b Immunofluorescence microscopic finding, C3 demonstrating marked deposition along the capillary wall in a granular pattern. $\times 400$.

1,170 mg/l, respectively), and cryoglobulin was not detected. Circulating immune complex containing IgA was not detected. A renal biopsy specimen showed mesangial proliferation and capillary wall thickening which are compatible with typical MCGN in all of

5 glomeruli by light microscopy (fig. 1a), marked glomerular deposition of IgM and C3 along the capillary wall in a granular pattern, and mild deposition of IgA (fig. 1b). She was treated with prednisone (2 mg/kg/day p.o. for 4 weeks, subsequently tapered over 5 weeks

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because of an increased risk of bacterial infection of the biliary tract). Two months later, her proteinuria decreased to 2.8-5.6 g/day, and the complement levels returned to normal (C3 910, C4 270 mg/l), although hypoproteinemia continued (serum total protein 50 g/l, serum albumin 27 g/l). It seemed that her hypoproteinemia was greatly due to impaired hepatic synthesis.

It has been reported that HGN can develop in childhood [1-3], although its reported histology is not consistent in these reports. We currently cannot conclude which is the more common finding in this condition: mesangial proliferative glomerulonephritis with IgA deposition of MCGN [2]. The duration affected by ESLD might be associated with the histology: the longer the period affected by ESLD, the more intense the MCGN. In fact, Ohtomo et al. [3] have reported that moderate to marked

mesangial proliferation with diffuse circumferential mesangial interposition is seen in older patients at autopsy. It is well known that idiopathic MCGN shows a worse outcome than idiopathic IgA nephropathy and Noble Jamieson et al. [2] reported that only 1 patient who showed clear long-term deterioration in renal function after liver transplantation had MCGN. Therefore, it seems important to investigate the kidney histologically in patients with ESLD and HGN, because renal involvement might affect the prognosis after liver transplantation. Furthermore, the recent controlled, double-blind trial of alternate-day prednisone for MCGN showed an improvement of the prognosis [4].

Our case together with this observation leads us to perform the control study on whether prednisone could be efficacious for children with MCGN caused by ESLD.

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