Nephrotic Syndrome in Non-Cirrhotic Portal Fibrosis: A Report of Three Cases

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Abstract
We describe three patients with nephrotic syndrome and non-cirrhotic portal fibrosis. In two of them, the liver disorder preceded the nephrotic syndrome while in the third patient the two conditions presented together. All the patients achieved remission of nephrotic syndrome with prednisolone and cyclophosphamide. Indian J Gastroenterol 1993; 12: 144-6

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Introduction
Glomerulonephritis has been described in more than 50% of patients with cirrhosis of liver. While it remains clinically silent in a majority of them, less than 2% present as nephrotic syndrome. Data on the incidence of glomerulonephritis in non-cirrhotic portal fibrosis (NCPF) are sparse. In one report from Delhi, 33% of patients with NCPF had histological evidence of glomerulonephritis prior to shunt surgery.

We report here three patients with nephrotic syndrome and NCPF, one of whom had undergone hilar shunt surgery 2 years prior to the development of nephrotic proteinuria.

Case Reports
Case 1: A 12 year old boy presented in December 1988 with abdominal distension. Clinical examination revealed moderate pallor and prominent periumbilical veins. The liver was just palpable below the right costal margin (span 10 cm) and had a rounded border. The spleen was palpable 8 cm below the left costal margin. There was no ascites and no free fluid in the abdomen.

Investigations revealed hemoglobin 11 g/dL with normal differential count. Liver function tests (LFT) were unremarkable and serum HBsAg, anti-HBc IgM and ANF were negative. Endoscopy revealed one grade II esophageal varix. Ultrasonography revealed hepatosplenomegaly and dilated portal vein (diameter 14 mm) with patent splenoportal system. Intrasplenic pressure was 20 mmHg. Liver biopsy showed features of NCPF. Routine urine examination was unremarkable.

He was followed up regularly without further deterioration till October 1990 when he developed swelling of the feet and face. Urine examination revealed proteinuria of 8 g/day, granular casts and RBC 2-3/HPF. Blood sugar, urea, creatinine and LFT were within normal limits. Renal biopsy revealed membranous nephropathy. The patient was treated with prednisolone and cyclophosphamide according to the Ponticelli regimen. He achieved remission of proteinuria in May 1991 and has remained relapse-free till January 1993.

Case 2: A 24 year old lady presented in January 1986 with abdominal swelling. Clinical examination revealed mild pallor, no ascites and no free fluid in the abdomen. Investigations revealed hemoglobin 12.5 g/dL with normal blood count. LFT, which showed increased globulin level (4 g/dL), was otherwise unremarkable. Serum HBsAg and anti-HBc IgM were negative. Ultrasonography showed evidence of portal hypertension (portal vein 15 mm) with patent splenoportal system and hepatosplenomegaly.
Urine routine examination was normal. Endoscopy revealed grade II esophageal varices. Intrapleural pressure was 19 mmHg. Liver biopsy was consistent with NCPF (Fig 1). The patient had episodes of upper gastrointestinal bleed in December 1986 and June 1987. In December 1987 she underwent distal ileo-renal shunt surgery. Urine examination was normal at that time. In June 1991 she developed generalized edema and received only diuretics.

In June 1992, her proteinuria was 6.5 g/day, urine RBC 2-3/HFP, with hyaline and granular casts in the urine. Serum total protein and albumin were 4.5 g/dL and 2.5 g/dL respectively. Blood sugar, urica, creatinine and LFT were within normal limits, A/NF and HBSAg were negative. Renal biopsy revealed membranous nephropathy (Fig 2). She has received prednisolone and cyclophosphamide every alternate month for 4 months so far. Urine analysis shows proteinuria 0.5 g/day and RBC 2-3/HPF; she is now edema-free without any diuretics.

Case 3: A 16 year old girl presented in January 1992 with generalized edema, hepatosplenomegaly and cervical lymphadenopathy of three weeks' duration. She was oliguric for 5 days prior to hospitalization. Examination revealed moderate right-sided pleural effusion, palpable liver (span 11 cm), smooth and soft with rounded margin, palpable spleen 9 cm below costal margin and free fluid in the abdomen. Peripheral blood count was unremarkable. LFT, which showed albumin of 2.5 g/dL, was otherwise unremarkable. HBSAg and anti-HBc IgM were negative. ANF was weekly positive but became negative after 1 month. Double stranded DNA was negative. Ultrasoundography showed evidence of portal hypertension (portal vein diameter 14 mm) with patent spleno-portal system and hepatosplenomegaly. Urine analysis showed proteinuria 4 g/day, RBC 6-8/HFP, with granular casts. Blood urea was 240 mg/dL and serum creatinine 10.2 mg/dL. Endoscopy revealed grade I to II esophageal varices. Intrapleural pressure was 20 mmHg.

Three sessions of hemodialysis were given. After 2 weeks she went into the diuretic phase and blood urea and serum creatinine improved to 16 mg/dL and 1.1 mg/dL respectively. Liver biopsy was suggestive of NCPF. Kidney biopsy showed features of membranoproliferative glomerulonephritis. Cerebral node biopsy showed reactive hyperplasia. She responded to cyclophosphamide 750 mg/m² IV every month for 3 cycles with oral prednisolone 10 mg/day. Her present urinalysis shows protein 1 g/day, RBC 2-4/HFP, blood urea 16 mg/dL and serum creatinine 0.8 mg/dL. Lymph nodes are not palpable but mild hepatomegaly and splenomegaly persist.

Discussion
The incidence and pathogenesis of glomerular disease in NCPF are unknown. It remains to be established whether the glomerular disease follows the same pattern as in cirrhosis of liver. In cirrhosis of liver, approximately 50% have histological evidence of glomerulonephritis. Mean glial IgA deposition is the most common (50%) abnormality. The renal lesion is clinically silent in the majority and nephrotic range proteinuria occurs in only 1.6% of cases. The pathogenesis of renal lesion in cirrhosis is thought to be related to defective hepatic processing and/or porto-systemic shunting of circulating immune complexes. Antigens derived from the gut and IgA antibody form complexes in the portal circulation; these bypass the liver in the presence of cirrhosis. Circulating IgA levels are elevated in 70-90% of patients of cirrhosis.

In NCPF, immune complexes which form in the portal circulation are likely to bypass the liver because of porto-systemic shunting even though Kupffer cell function, and hence hepatic processing, is relatively well preserved.

We are not aware of any report of nephrotic syndromes in NCPF. A study from Delhi reported histological evidence of glomerulo nephritis in as high as 33% of cases; however, clinical presentation prior to ileo-renal shunt surgery was not clearly mentioned. After shunt surgery, only 15% developed clinical and biochemical evidence of glomerulonephritis in a follow-up of up to 8 years. During this period, 6.6% of these patients died and 43.3% progressed to renal failure. The authors concluded that the results of therapy for glomerulonephritis were poor.

Our limited experience has shown that the results
of therapy for glomerulonephritis are not different from that in patients without NCPF. Further work is necessary to ascertain the incidence and pathogenesis of glomerulonephritis in patients with NCPF.

References

NEWS AND NOTICES

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