Minimal-change glomerulonephritis associated with infantile autosomal recessive polycystic kidney disease

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Introduction

Infantile autosomal recessive polycystic kidney disease (ARPKD) is a hereditary renal cystic disease in children with an estimated frequency of between 1:10,000 and 1:55,000 [1]. This disorder is transmitted as an autosomal recessive trait [2]. Proteinuria is frequently detected in these patients; however, it usually amounts to less than 3 g/day. We report on a 23-year-old female patient with ARPKD who developed nephrotic range proteinuria because of minimal-change glomerulonephritis.

Case report

A 23-year-old caucasian woman was diagnosed as having infantile ARPKD in 1975 as an incidental finding after having a thorough examination because of suspected pertussis. The family history revealed that a paternal uncle died of renal failure some years ago and was said to have cysts in both kidneys. The parents and the brother of the patient were in a healthy condition. In 1978 splenomegaly had been noted by sonography. Liver and spleen scan at that time demonstrated splenomegaly with uniformly increased tracer uptake. Routine biochemical and haematological tests were normal; serum creatinine was 0.9 mg/dl, and creatinine clearance was slightly decreased to 65 ml/min.

At age of 15 the patient presented with hypersplenism, thrombocytopenia (platelet count 60,000/µl), and recurrent epistaxis. A bone-marrow aspiration revealed a normal function with hypoplasia of granulopoiesis, which was interpreted as splenogenic inhibition. A malignant systemic disease could be excluded as the cause of thrombocytopenia. In February 1989, splenectomy was performed with concomitant tonometry of portal vein and open biopsy of the liver. The histomorphological examination revealed congenital hepatic fibrosis with cirrhotic transformation. The portal vein pressure was 17 mm H$_2$O. Collateral circulation as a sign of portal hypertension was found; endoscopic examination showed no gastric or oesophageal varices.

In September 1995 the patient became pregnant. During pregnancy kidney function remained stable. Creatinine clearance remained between 60 and 75 ml/min and serum creatinine between 0.9 mg/dl and 1.3 mg/dl. Proteinuria was highest with 0.2 mg/24 h. In May 1996 the patient had a full-term normal delivery. In January 1997 she developed a nephrotic syndrome with proteinuria of 16 g/24 h, oedema of the legs and weight gain of 4 kg. Serum albumin and total protein content were markedly reduced and serum lipids increased. Creatinine clearance decreased to 42 ml/min. At that time serum creatinine was 1.7 mg/dl. A kidney biopsy was performed. Light-microscopy revealed normal glomeruli. Immunofluorescence microscopy was negative for immunoglobulins and complement but demonstrated mild, focal deposits of IgM in the mesangium. Electron-microscopy showed unaffected glomerular basement membranes but fusion of the podocyte foot processes. Minimal-change glomerulonephritis was diagnosed. Malignancy, non-steroidal anti-inflammatory drugs, ampicillin, the use of gold, lithium, or mercaptopropionylglycine as possible causes of minimal-change glomerulonephritis could be excluded.

A standard prednisone regime, beginning with 1 mg/kg body weight/day, was started. Three months later proteinuria disappeared and creatinine clearance slightly increased; serum creatinine declined to 1.4 mg/dl.

Discussion

The clinical spectrum of ARPKD is variable and also the prognosis relating to the extent of renal and hepatic
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Involvement. Renal failure and hepatic cirrhosis, due to cysts and fibrosis, frequently develop and are the major causes of death. Until now the pathogenesis of ARPKD remains unclear. Linkage analysis has allowed workers to map the gene for ARPKD to chromosome 6p [3]. Life-table survival rates calculated from birth revealed that 46% of the patients with ARPKD were alive at 15 years [4].

In polycystic kidney disease (PKD) glomerulonephritis is thought to occur only rarely [5]. Only a few PKD patients have been seen with different glomerular abnormalities such as rapidly progressive glomerulonephritis [6], focal glomerulosclerosis [7], membranous glomerulonephritis [8], IgA nephropathy [9] or membranoproliferative glomerulonephritis [10]. Low-degree proteinuria is observed in many patients with PKD [11,12]. Todorov and co-workers [13] observed 152 patients of 51 families and found no case of proteinuria above 3 g/l urine nor a nephrotic syndrome. All the cases presenting with heavy proteinuria or nephrotic syndrome had either advanced renal failure or an accompanying increase in the rate of decline in renal function.

We present, to our knowledge, the first patient with ARPKD associated with minimal-change glomerulonephritis and nephrotic syndrome which responded to steroid therapy.

References


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