Massive Proteinuria and Autosomal Dominant Polycystic Kidney Disease
A Rare Coincidence

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Autosomal dominant polycystic kidney disease (ADPKD) with nephrotic syndrome is a rare coincidence. Among 19 reported cases since 1972, focal glomerulosclerosis is the dominant reported pathology. Here, we report the 6th case of focal segmental glomerulosclerosis with ADPKD. A 29-year-old man with a history of APCDK presented with massive proteinuria. He had a history of concurrent leptospirosis and brucellosis, and trace proteinuria and mild hypertension had been diagnosed 4 years earlier. Urine study showed proteinuria (21 g/d) and hematuria. Kidney biopsy report was compatible with focal and segmental sclerosis. The patient received prednisolone and cyclosporine. After 4 months, proteinuria decreased to 600 mg/d. Patients with ADPKD who show massive proteinuria should undergo kidney biopsy. It is possible that different mutations in these patients could clarify the nature of this coincidence.

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INTRODUCTION

Non-nephritic range proteinuria is a common presentation in autosomal dominant polycystic kidney disease (ADPKD) patients; however, nephrotic syndrome is a rare coincidence. There are only 19 cases of such coincidence since 1972. Among different histopathologies including focal glomerular sclerosis (FGS), membranous glomerulonephritis, immunoglobulin A nephropathy, amyloidosis and mesangioproliferative glomerulonephritis, FGS is the dominant pathologic finding, which has been reported in 5 cases.[1] Here, we report the 6th case of ADPKD with massive proteinuria and FGS on kidney biopsy.

CASE REPORT

A 29-year-old man with a history of polycystic kidney disease was admitted to Firoozgar General Hospital in March 2010 with massive proteinuria. At the beginning of the year, he sought for medical advice because of periorbital and extremities edema, ascitis, and dyspnea. The diagnosis of ADPKD had been made 6 years earlier, when he had been admitted to hospital because of fever, icter, and abdominal pain. During that period of admission the diagnosis of brucellosis and leptospirosis had been made for him and he had been treated with antibiotics. Abdominal ultrasonography had shown multiple cysts in both kidneys. He had a family history of ADPKD in his mother and aunt. After discharge from hospital, there had been no sign of proteinuria and renal impairment in 2-year follow-up. Four years earlier, his urinalysis showed the first sign of trace proteinuria and high blood pressure. After complete workup for secondary glomerulonephritis, he was treated by angiotensin receptor blockers, but he did not come for follow-up for 4 years.

He had no sign of gross hematuria, sore throat, skin infection, skin rash, or oral ulcers and was not on any medications. Physical examination findings were anasarca, a blood pressure of 140/90 mm Hg,

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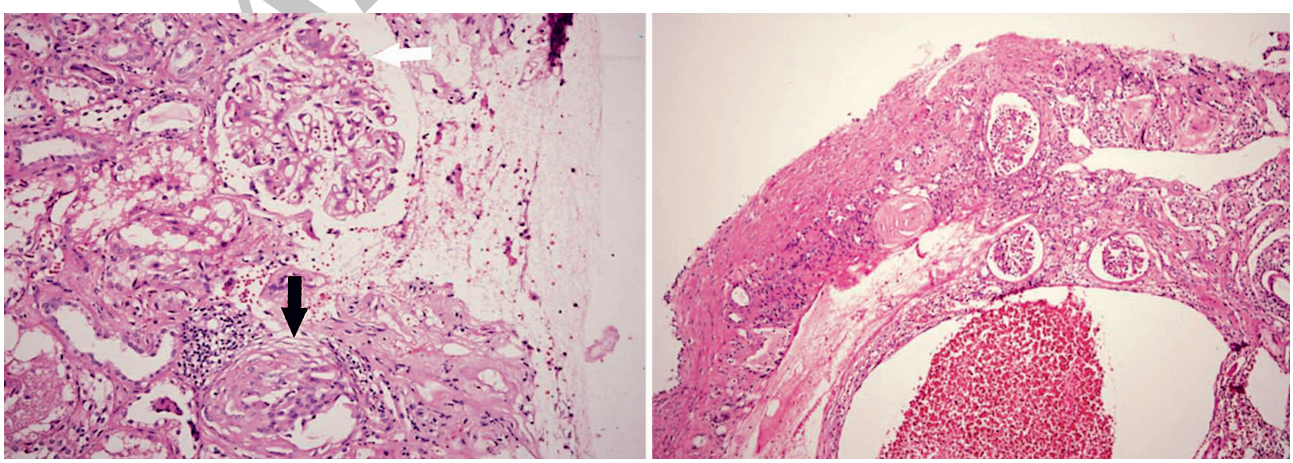
a body weight of 102 kg, and a body mass index of 28.25 kg/m^2. Laboratory investigations showed massive proteinuria (21 g/d) and microscopic hematuria (5 to 6 erythrocytes per high-power field). None of the studies for secondary glomerular disease were significant (Table). Kidney ultrasonography showed polycystic kidneys. The right kidney sized 159 × 62 mm and the left kidney was 203 × 75 mm with normal flow on Doppler ultrasonography of the vessels. The other pathologic report on abdominal spiral computed tomography (without contrast) was ascites.

The patient underwent open kidney biopsy, and the specimen was processed for immunofluorescence and light microscopy studies. There was no immunoglobulin, complement C1q, complement C3c, complement C4c, fibrinogen, or albumin on immunofluorescence study. On light microscopy study, there were 50 glomeruli, of which 6 were small and sclerotic. Six glomeruli had segmental sclerosis and synechia. About 10% of the glomeruli were simplified glomeruli. There were some cystic tubules, and some other tubules were preserved and showed absorptive changes. About 30% of the specimen showed fibrotic interstitium with patchy infiltration of mononuclear cells. The vessels showed no pathologic changes. No amyloid deposition was observed on Congo-Red stained slides with polarized microscopy (Figure). Regarding these findings, a diagnosis of focal segmental glomerulosclerosis in the background of cystic kidney disease was made. The patient was treated with prednisolone, 65 mg/d, and cyclosporine, 3 mg/kg/d. After 4 months, proteinuria decreased to 600 mg/d.

Laboratory Data*

Test	Result
Complete blood count	
Leukocyte, × 10^9/L	9.1
Hemoglobin, g/dL	14
Platelet, × 10^9/L	175
ESR, mm/h	32
Urinalysis	
Protein	3+
Leukocyte, /HPF	0 to 1
Erythrocyte, /HPF	6 to 8
Urine Protein, g/24 h	21.6
Blood urea nitrogen, mg/dL	26
Serum creatinine, mg/dL	1.1
Serum cholesterol, mg/dL	394
Serum triglyceride, mg/dL	271
Serum LDLC, mg/dL	190
Serum HDLC, mg/dL	54
Serum calcium, mg/dL	8.5
Serum albumin, g/dL	2.1
C-reactive protein	Negative
Hepatitis B surface antigen	Negative
Hepatitis C antibody	Negative
Antinuclear Antibody	Negative
Perinuclear ANCA	Negative
Cytoplasmic ANCA	Negative
Liver function tests	Normal
Thyroid function tests	Normal
Protein electrophoresis, g/dL	0.49
Tuberculosis skin test, mm	5
Wright	Negative
VDRL	Negative
Rheumatoid factor	3+
Complement C3, mg/dL	163
Complement C4, mg/dL	30
CH50, %	96

*ESR indicates erythrocyte sedimentation rate; HPF, high-power field; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; ANCA, antineutrophil cytoplasmic antibody; VDRL, venereal disease research laboratory; and CH50, total complement activity.



Left, One sclerotic glomerulus (black arrow) adjacent to the glomerulus with segmental sclerosis (white arrow; hematoxylin-eosin, × 400). **Right,** Four glomeruli with a cyst lined with flat epithelium (hematoxylin-eosin, × 40).

DISCUSSION

Autosomal dominant polycystic kidney disease is a common disorder, occurring in approximately 1 in every 400 to 1000 live births. It is estimated that less than one-half of the cases will be diagnosed during the patient's lifetime, as the disease is often clinically silent.[3,4] Massive proteinuria is an uncommon finding in a patient with ADPKD. There were only 19 cases of such coincidence since 1972 the literature, and our report is the 20th one.[1] The frequency of occurrence of non-nephrotic proteinuria in ADPKD ranged from 14% to 34% in nonuremic adults to about 80% in adults with advanced kidney failure.[1] When present in patients with ADPKD, proteinuria is generally less than 1 g/24 h.[2] In a literature review, we found that only 4 reported cases had signs of nephritic-range proteinuria and progressive kidney failure resistant to treatment. Two patients underwent dialysis in 6 years. The age range of these patients was 35 to 65 years.[5-8] In contrast, our patient was 25-year-old when he first showed signs of proteinuria. Proteinuria increased during 4 years, and after open kidney biopsy and starting treatment with steroids and cyclosporine, proteinuria decreased dramatically. His plasma creatinine did not increase even when he had 21 g/d proteinuria which was against what had already reported.

The various histopathological lesions reported in ADPKD patients are FSG, membranous nephropathy, minimal change disease, crescentic glomerulonephritis, immunoglobulin A nephropathy, mesangioproliferative glomerulonephritis, diabetic glomerulosclerosis, and amyloidosis.[2] Among the 20 reported cases, 5 (including ours) have been reported to have pure focal segmental glomerulosclerosis lesions. Although the etiologic classification of FGS is complicated and somewhat confusing, with some degrees of overlap observed among the different categories, it is usually classified as primary and secondary FGS. Primary FGS may respond to immunosuppressive agents such as corticosteroids, while secondary FGS often fails to respond to corticosteroids and may be best treated with modalities aimed at lowering the intraglomerular pressure, such as angiotensin-converting enzyme inhibitors. In contrast to patients with secondary FGS who present with slowly increasing proteinuria and renal insufficiency over time, patients with primary FGS more typically present with the acute onset of the nephrotic syndrome. Primary FGS is also associated with peripheral edema, hypoalbuminemia, and usually, nephritic-range proteinuria. By comparison, proteinuria in secondary FGS is often non-nephrotic, and both low serum levels of albumin and edema are unusual even when protein excretion exceeds 3 g/d to 4 g/d.[9,10]

According to the current knowledge about FSGS and our findings about current and previous cases, the FGS type in ADPKD is more correspondents to primary FGS than the secondary type. Based on these findings, this hypothesis can be presented that coincidence of ADPKD and FGS can be caused by 2 independent concurrent genetic mutations in patients' chromosome which are not necessarily related or one single mutation, which is unknown yet. Based on the type of this mutation, disease course can be changed. According to this report, we recommend that ADPKD patients who show massive proteinuria undergo kidney biopsy. It is possible that different mutations in these patients could clarify the nature of this coincidence.

CONFLICT OF INTEREST

None declared.

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