Coexistence of Autosomal Dominant Polycystic Kidney Disease and Amyloidosis in a Patient With Nephrotic-range Proteinuria

Ezgi Coskun Yenigun, Fatih Dede, Nihal Ozkayar, Didem Turgut, Serhan Vahit Piskinpasa, Ramazan Ozturk, Eyup Koc, Ali Riza Odabas

Department of Nephrology, Ankara Numune Research and Education Hospital, Ankara, Turkey

Keywords. amyloidosis, nephrotic syndrome, polycystic kidney disease, proteinuria

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disorder characterized by the development and growth of cysts in the kidneys. Non-nephritic-range proteinuria is a common presentation in ADPKD patients; however, nephrotic syndrome is a rare coincidence. A 52-year-old man is described who was diagnosed with secondary amyloidosis with ADPKD. To our knowledge, this is the first case of amyloidosis associated with frequently infected renal cysts. Patients with ADPKD who show massive proteinuria should be investigated in terms of concomitant glomerular disease.

IJKD 2014;8:243-5
www.ijkd.org

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is characterized by multiple cysts in the cortex and medulla. Although moderate proteinuria is frequent, nephrotic proteinuria is rare and should suggest the presence of concomitant glomerular disease. The various histopathological lesions reported in ADPKD patients are focal segmental glomerulosclerosis (FSGS), membranous glomerulonephritis, imunoglobulin A nephropathy, amyloidosis, diabetic glomerulosclerosis and mesengioproliferative glomerulonephritis.[1] In a literature review, we found that only 3 reported cases had amyloidosis due to recurrent hepatic cyst infection and pulmonary tuberculosis. Here, we describe a patient with ADPKD associated with nephrotic syndrome due to amyloidosis secondary to recurrent renal cyst infection.

CASE REPORT

A 52 year-old man with a history of ADPKD was admitted to our hospital with vomiting and nausea. The diagnosis of ADPKD had been made 10 years earlier when he had been admitted to hospital because of fever and abdominal pain. During that period, the diagnosis of upper urinary tract infection had been made for him and he had been treated with antibiotics many times in our hospitals. He had a family history of ADPKD in his mother. Five months ago there was a moderate elevation of creatinine; however, he had not undergone proteinuria examination. On clinical history, there were no history of tuberculosis, inflammatory bowel disease, familial mediterranean fever (FMF), or lung and rheumatic disease. He had no sign of gross hematuria, skin infection, skin rash, fever, oral ulcers, joint pains, edema, or rash.

On physical examination, his blood pressure was 120/80 mm Hg, pulse rate was 82 per minute, and body temperature was 36.5°C, while the examinations of other systems proved normal. The laboratory examination showed a serum urea level of 162 mg/dL (reference range, 10 mg/dL to 50 mg/dL); serum creatinine, 8.1 mg/dL (reference range, 0.6 mg/dL to 1.3 mg/dL); serum potassium, 3.9 mmol/L (reference range, 3.5 mmol/L to 5.5

Case Report

mmol/L); serum total protein, 52 g/L (reference range, 64 g/L to 83 g/L); serum albumin, 12 g/L (reference range, 35 g/L to 54 g/L); eritrocyte sedimentation rate (ESR), 64 mm/h; C-reactive protein, 15 mg/L (reference range, zero to 5 mg/L); hemoglobin: 9.9 g/dL; leukocyte count, 11×10^9/L; and platelet count, 304×10^9/L. Other hematologic and biochemical parameters were normal. Automatic full urine testing showed a urine protein level of 100 mg/dL, and the sediment contained erythrocyte, 1 to 2 per high-power field. Daily urinary protein excretion was 11 g/24 h. Urine culture was negative. Serum complement C3, C4, immunoglobulin A, immunoglobulin G, and immunoglobulin M levels were normal. Tests for hepatitis A and C, human immunodeficiency virus, antinuclear antibody, anti-DNA, rheumatoid factor, and anti-neutrophil cytoplasmic antibodies were all negative. Abdominal ultrasonography examination revealed enlarged kidneys with bilateral multiple cysts, and some cysts showed granuler pattern.

Due to the nephrotic-range proteinuria, ultrasound-guided renal biopsy was made. Biopsy revealed Congo-positive amyloid deposition, and immunoperoxidase technique showed amyloid A component. Since the most common diseases associated with amyloid A amyloidosis are FMF, tuberculosis, bronchiectasis, rheumatoid arthritis, spondyloarthropathy, and chronic osteomyelitis in our country, further evaluation was made to find out the underlying inflammatory disease. The patient denied any gastrointestinal symptoms, fever, coughing, night sweat, weight loss, or production of sputum. He did not have morning stiffness, neck or back pain, swelling, or tenderness localized to any of the joints. No findings of arthritis and no rheumatoid nodules were observed. There were no limitations of anterior and lateral flexion and extension of the lumbar spine and of chest expansion. Chest radiography did not show infiltrates or cavities consistent with tuberculosis. Skin testing for tuberculosis was negative. High-resolution computed tomography scan was not suggestive of bronchiectasis or other lung pathologies. Although the patient did not have a family history or clinical characteristics and symptoms of FMF, genetic testing was performed which revealed no FMF gene mutations. Since the patient did not have any of the chronic inflammatory diseases which may potentially lead to secondary amyloidosis, a diagnosis of ADPKD with amyloid A amyloidosis was made. The patient was followed up with colchicine at a dose of 0.5 mg/d and hemodialysis.

DISCUSSION

Autosomal dominant polycystic kidney disease is a disease characterized by multiple cyst formation in the kidney.[1] It may affect all segments of the nephron, including the proximal tubule; but it has not been addressed whether alterations of this nephron segment contribute to proteinuria and albuminuria.[2] The urinary excretion of protein is usually less than 2 g/24 h and 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.[3] The nephrotic-range proteinuria observed in some patients with ADPKD could be the consequence of other superimposed glomerular diseases. Since there is no apparent pathogenic link between ADPKD and the different causes of nephrotic syndrome that have been reported in ADPKD patients, it suggests that they are likely coincidental diseases.

In 1957, Dalgaard described three instances of nephrotic-range proteinuria in a report reviewing 122 patients with ADPKD, but renal biopsy data were not included.[4] Almost every form of primary glomerulopathy has been reported in ADPKD. Among different histopathology, FSGS is the dominant pathologic finding.[3] The high frequency of FSGS suggests that the glomerular hemodynamic changes induced in ADPKD and the formation of FSGS may play an important role in the progression to end-stage renal disease in a subgroup of ADPKD patients.[5]

Polycystic kidneys have increased susceptibility to infections; incidence of infection has been reported as 21% to 69%.[6] Amyloidosis can be seen in course of the disease due to recurrent cyst infections that stimulating chronic inflammatory response. Secondary amyloidosis is the most frequent type of systemic amyloidosis and is a frequent complication in severe chronic infectious and inflammatory states. Cases of ADPKD with amyloidosis associated with frequent episodes of cyst infection in the liver and tuberculosis were described in the literature.[7-9] One of these reports the authors presented a case with diarrhea due to amyloidosis and an endoscopic biopsy was

performed for diagnosis.[9] Our patient had nephrotic range proteinuria and we performed renal biopsy to exclude concomitant glomerular disease. He was diagnosed amyloidosis. It is well known the relationship between amyloidosis and chronic infections. The patient had a history of recurrent upper urinary tract infection which might have contributed to the development of amyloidosis.

Most of clinicians avoid percutaneous renal biopsy because of large cysts presumed risk of complications and difficulties in obtaining suitable tissue for diagnosis. The evaluation of the data of these patients also revealed that only anecdotal case reports of ADPKD received an ultrasound- or computed tomography-guided percutaneous renal biopsy, while the remaining patients received an open surgical biopsy.[1,5,10-13] There is no strict contraindication for renal biopsy in ADPKD patients with nephrotic syndrome. This case supports the idea that renal biopsy is needed in patients with polycystic kidney disease with nephrotic-range proteinuria, for appropriate treatment.

In summary, nephrotic syndrome occurs in a minority of ADPKD patients and its presence defines severe renal involvement both structurally and functionally. The clinical data of ADPKD patients with nephrotic syndrome suggests that they show faster progression to end-stage renal disease than ADPKD patients without nephrotic syndrome and the appearance of nephrotic-range proteinuria indicates the presence of treatable superimposed glomerular lesions; thus, renal biopsy should be recommended in such patients.[5]

Our patient had ADPKD and the signs of nephrotic syndrome. We assessed that secondary amyloidosis was the main etiological cause for his nephrotic syndrome. We speculate that amyloidosis may be secondary to recurrent cysts infection associated inflammation observed in the present case, and thought that these two pathologies were coincidental.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Hiura T, Yamazaki H, Saeki T, et al. Nephrotic syndrome and IgA nephropathy in polycystic kidney disease. Clin Exp Nephrol. 2006;10:136-9.
2. Simon HB, Thompson GJ. Congenital renal polycyctic disease. JAMA. 1955;159:657.
3. Chapman AB, Johnson AM, Gabow PA, Schrier RW. Overt proteinuria and microalbuminuria in autosomal dominant polycystic kidney disease. J Am Soc Nephrol. 1994;5:1349-54.
4. Dalgaard OZ. Bilateral polycystic disease of the kidneys; a follow up of 284 patients and their families. Acta Med Scand. 1957;158:1-255.
5. Contreras G, Mercado A, Pardo V, Vaamonde CA. Nephrotic syndrome in autosomal dominant polycystic kidney disease. J Am Soc Nephrol. 1995;6:1354-9.
6. Obermuller N, Kranzlin B, Blum WF, Gretz N, Witzgall R. An endocytosis defect as a possible cause of proteinuria in polycystic kidney disease. Am J Physiol Renal Physiol. 2001;280:244-53.
7. Kamimura H, Tsuchiya K, Honda K, et al. Secondary systemic amyloidosis associated with frequently infected hepatic cysts in a patient with autosomal dominant polycystic kidney disease. Clin Nephrol. 2003;59:485-8.
8. Sar F, Taylan I. Amyloidosis in a patient with autosomal dominant polycystic kidney disease and tuberculosis: a case report. Int Urol Nephrol. 2007;39:655-9.
9. Tsuchiya Y, Ubara Y, Suwabe T, et al. AA-amyloidosis in Autosomal Dominant Polycystic Kidney Disease Caused by Chronic Cyst Infections Lasting for 30 years. Intern Med. 2013;52:791-4.
10. Wan RK, Kipgen D, Morris S, Rodger RSC. A rare cause of nephrotic syndrome in autosomal dominant polycystic kidney disease. Nephrol Dial Transplant Plus. 2009;2:136-8.
11. Kengne-Wafo S, Massella L, Diomedi-Camassei F, Emma F. Idiopathic membranous nephropathy associated with polycystic kidney disease. Pediatr Nephrol. 2010;25:961-3.
12. D'Cruz S, Singh R, Mohan H, et al. Autosomal dominant polycystic kidney disease with diffuse proliferative glomerulonephritis - an unusual association: a case report and review of the literature. J Med Case Rep. 2010;4:125.
13. Savaj S, Parvin M, Savoj J. Massive proteinuria and autosomal dominant polycystic kidney disease: A Rare Coincidence. Iran J Kidney Dis. 2012;6:73-6.

Correpsondence to:
Ezgi Coskun Yenigun, MD,
Department of Nephrology, Ankara Numune Research and Education Hospital, Ankara Numune Eğitim ve Araştırma Hastanesi Nefroloji Kliniği, 06100, Samanpazarı, Ankara, Turkey
Tel: +90 312 508 45 52
Fax: +90 312 310 46 16
E-mail: drezgi_76@hotmail.com

Received May 2013
Revised September 2013
Accepted September 2013