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The Diagnosis of Lupus Nephritis in A Patient with Autosomal Dominant Polycystic Kidney Disease: A Rare Case Report

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Case Report

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Autosomal dominant polycystic kidney disease (ADPKD), as a widespread inherited cystic kidney disease has a prevalence of ~1/1000 live births. However, there are rare reports of the association of ADPKD with nephrotic range proteinuria such as lupus nephritis (LN). In this study, we report a patient with ADPKD who manifested a sudden increase of urinary protein excretion with positive anti-double stranded DNA and antinuclear antibody tests. Finally, based on percutaneous ultrasound-guided renal biopsy LN was proved. This report advises clinicians to evaluate ADPKD patients periodically and perform complementary clinical and laboratory investigations in cases with unusual presentations such as nephrotic syndrome.

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INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is a common genetic renal disease, featured by the formation of several renal cysts that can ultimately lead to kidney failure.[1] Total worldwide incidence of ADPKD is approximately 12.5 million individuals.[2] Lupus nephritis (LN) is the most common form of secondary glomerulonephritis.[3] The overall incidence of LN varies depending on factors such as, geography and ethnicity, ranging from 0.3 to 23.2 cases per 100,000 individuals.[4] According to the classification of the International Society of Nephrology/Renal Pathology Society (ISN/RPS), active LN is characterized by proliferative lesions (classes III or IV), or intramembranous immune complex deposits (Class V).[5]

Patients with ADPKD may rarely manifest with nephrotic range proteinuria, as reported in previous studies.[6,7] Among these, only seven cases of coexisting ADPKD and LN have been reported.[8-14] Here, we present a known case of ADPKD, with a history of discoid lupus erythematosus, who presented with generalized edema and nephrotic range proteinuria.

CASE REPORT

The patient was a 42-year-old man with a known diagnosis of ADPKD, and a positive family history of the disease, referred for a rise in serum creatinine, to Hasheminejad Kidney Center, Tehran. He had bilateral erythematous, non-itching plaques on his face, shoulders, and chest dating back to six years ago, together with photosensitivity. He had been diagnosed with cutaneous lupus, confirmed by skin biopsy. On admission, the patient complained of abdominal distention, later diagnosed as ascites, and generalized edema since the last month. He had a reduced kidney function with a baseline serum creatinine of 1 mg/dL, increasing to 4.8 mg/dL at presentation. In further evaluation he had a 24 hour urine of 6744 and positive anti-double stranded DNA (anti-dsDNA) and antinuclear antibody (ANA) tests (Table 1).

Table 1. Clinical information of the reported case

Parameter	Value
Complete blood count	
HCT (%)	32.5
Hemoglobin (g/dL)	11.3
MCH (pg)	30.46
WBC (10^9/L)	16.8
RBC (10^9/L)	3.71
Platelet (10^9/L)	140
Lymphocyte (10^9/L)	1.9
Neutrophil (%)	96.1
RDW (%)	16.3
Electrolytes	
Sodium (mg/dL)	140
Potassium (mg/dL)	3.4
Magnesium (mg/dL)	2.15
Phosphorus (mg/dL)	6.4
Calcium (mg/dL)	8
Immunology analysis	
C3 (g/L)	0.91
C4 (g/L)	0.31
CH50 (U/mL)	101
ANA (AU/mL)	2
ANCA	Negative
Anti-dsDNA (IU/mL)	2.1
Hormone analysis	
PT (seconds)	12
PTT (seconds)	26
PTH (pmol/L)	113

Parameter	Value
Biochemical analysis	
Serum creatinine (mg/dL)	4.8
Proteinuria (mg/day)	6744
Ferritin (ng/dL)	571
Serum Iron (µg/dL)	62
TIBC (µg/dL)	303
Triglyceride (mg/dL)	495
Cholesterol (mg/dL)	313
HDL-C (mg/dL)	61
LDH (U/L)	599
LDL-C (mg/dL)	182
ALP (U/L)	119
ALT (U/L)	30
AST (U/L)	30
Direct bilirubin (mg/dL)	0.21
Total bilirubin (mg/dL)	0.54
Uric acid (mg/dL)	7.8
Albumin (mg/dL)	3.4
BUN (mg/dL)	71
CRP (mg/dL)	0.8
ESR 1 hour (mm/h)	24
Medication	
Methylprednisolone	500 mg/day for 3 days
Cyclophosphamide	750 mg single dose

ALP: Alkaline Phosphatase, ALT: Alanine aminotransferase, ANA: Antinuclear antibody, ANCA: Anti-neutrophil cytoplasmic antibody, anti-dsDNA: anti-double stranded DNA, AST: aspartate aminotransferase, BUN: blood urea nitrogen, CRP: C-reactive protein, ESR: estimated sedimentation rate, HCT: Hematocrit, HDL: High-density lipoprotein, LDH: Lactate dehydrogenase, LDL: Low-density lipoprotein, MCH: Mean corpuscular hemoglobin, PT: Prothrombin time, PTH: Parathyroid hormone, PTT: Partial prothrombin time, RBC: Red blood cell, RDW: Red cell distribution width, TIBC: total iron binding capacity, WBC: White blood cell.

Due to the presence of severe proteinuria and a rise in serum creatinine, the patient was admitted for a kidney biopsy. Initially, an ultrasound of the kidneys was performed, showing the sizes of the left and right kidneys as 144 and 131 mm, respectively. The diagnosis of polycystic kidney disease was approved according to the existence of numeric corticomedullary cysts at the upper, middle, and the lower poles of both kidneys. The size and number of cysts in the left kidney were larger, with a maximum diameter of 47 mm (Figure 1).

Consequently, following one session of hemodialysis, a percutaneous ultrasound-guided kidney biopsy was performed on the lower pole of the right kidney, where the cysts were fewer and smaller in size. There were three pieces of renal cortex and one piece of corticomedullary tissue, totally containing 51 glomeruli. The pathology result reported diffuse proliferative glomerulonephritis, consistent with diffuse LN (ISN/RPS IV-G (A/C)

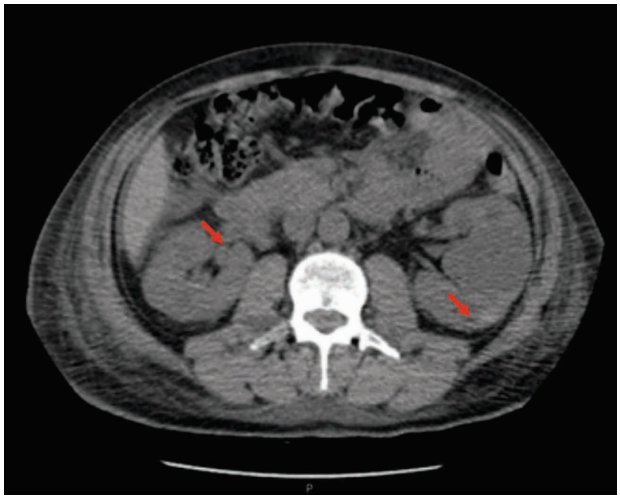

Figure 1. The CT scan of patient's kidney. The cysts are shown by red arrows.

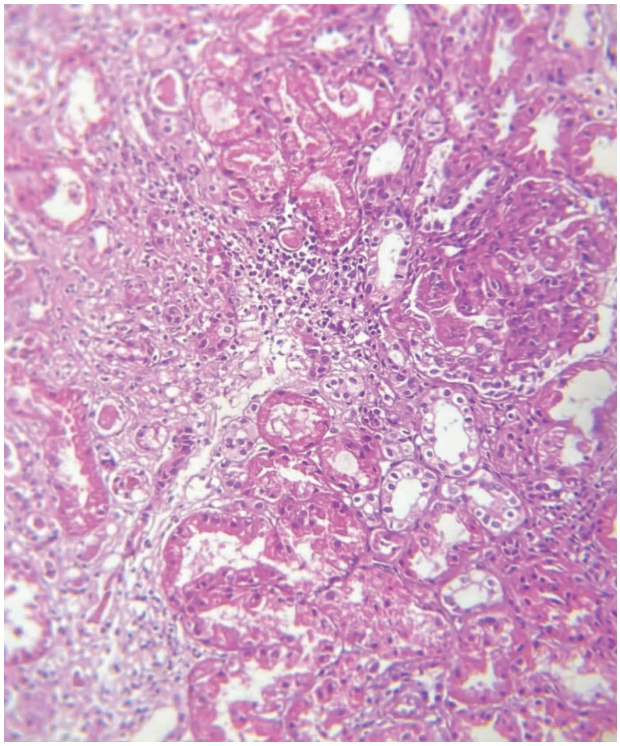

Figure 2. Pathology slide of the patient's kidney biopsy. (H&E stain, ×100)

with moderate activity (15 cellular and fibro-cellular crescents) and chronicity (4 segmentally and 20 globally sclerotic glomeruli with 3 fibrous crescents and 30% tubular fibrosis and interstitial atrophy), with relevant indices of 11/24 and 6/12 (Figure 2).

The patient was treated with three consecutive daily doses of 500 mg intravenous (IV) Methylprednisolone pulse and 750 mg of IV Cyclophosphamide. He was discharged with a serum creatinine level of 4.2 mg/dL, but unfortunately did not return for follow-up. Additional information is provided in Table 1.

DISCUSSION

In this case report we describe a patient with ADPKD, referred due to nephrotic range proteinuria, and a significant rise in serum creatinine, who had positive ANA and anti-dsDNA tests and was finally diagnosed with LN. He was treated with Methylprednisolone and Cyclophosphamide, which resulted in a primary reduction in serum creatinine.

While mild proteinuria, usually less than 1g/day, is common among patients with ADPKD, nephrotic range proteinuria is rarely seen in these patients and few studies have reported ADPKD cases complicated with nephrotic syndrome.[7,15] In the study conducted by Visciano *et al*, 29 ADPKD patients with nephrotic syndrome were evaluated through kidney histopathology.[6] To the best of our knowledge, only seven case reports have diagnosed ADPKD patients with LN worldwide.[16] One confirmed case of LN was established via percutaneous renal biopsy, conducted before the detection of renal cysts on ultrasound, and the reactivation of LN was noted with nephrotic range proteinuria along with the diagnosis of ADPKD.[8] Another case of ADPKD with initially negative ANA, was diagnosed as LN through CT-guided renal biopsy.[9] Likewise, a young female patient was observed with inherited ADPKD, glomerular proteinuria, and red blood cell casts, who was consequently diagnosed as LN, with no association between the two diseases.[10] Another study reported a 24-year-old female patient with a positive anti-dsDNA antibody and an ISN/RPS II LN, co-existing with ADPKD.[11] Moreover, a study reported two patients with simultaneous ADPKD and LN with lymphopenia, proteinuria (0.68 g/day), positive ANA (1/200), and positive Anti-Smith antibody. A renal biopsy was not performed because of the presence of multiple cysts in the kidney.[12] Park *et al.* reported another patient with ADPKD who underwent laparoscopic renal biopsy and was diagnosed as having LN.[13] Urinalysis is typically performed for ADPKD patients and the diagnosis is often based on family history and imaging studies without any need for renal biopsy, which has a higher potential for being complicated in these patients.[8] However, ADPKD patients with nephrotic-range proteinuria and/or sudden serum creatinine rise should be completely assessed to diagnose any added kidney disease, complicating the underlying condition and may need to undergo a kidney biopsy with very careful measures implied for prevention of cyst rupture and massive hemorrhage.

CONCLUSION

There are few reported patients with ADPKD and lupus nephritis, but to the best of our knowledge, this is the first report of a patient with ADPKD who was diagnosed with LN in Iran. Appropriate therapy of LN can change the prognosis of such patients and the nephrologists should perform periodic evaluations in ADPKD patients, being aware of possible secondary complicating conditions. As these patients may have hematuria due to cyst

hemorrhage, it is important to pay attention to proteinuria out of the context of hematuria and/or a rapid rise in serum creatinine, and consider additional investigations in cases of high clinical suspicion, especially in the presence of nephrotic range proteinuria.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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INFORMED CONSENT

Written consent was obtained from the patient.

ETHICAL CONSIDERATIONS:

This study was approved with ethical code IR.IUMS.FMD.REC.1404.058 in Iran University of Medical Sciences.

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