Case Report

Laparoscopic biopsy-proven lupus nephritis in autosomal dominant polycystic kidney disease

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Abstract

A 48-year-old woman with autosomal dominant polycystic kidney disease (ADPKD) presented with generalized edema and arthralgia. She showed evidences of acute glomerulonephritis including nephrotic-ranged proteinuria. Because her serologic test results were consistent with those for systemic lupus erythematosus (SLE), we performed laparoscopic renal biopsy that confirmed World Health Organization (WHO) class IV lupus nephritis. She was treated with steroids and intravenous cyclophosphamide pulse therapy and eventually started hemodialysis 8 years after the lupus nephritis was diagnosed. To our knowledge, this is the first case wherein a patient with ADPKD underwent a laparoscopic biopsy for diagnosing lupus nephritis.

Introduction

In patients with autosomal dominant polycystic kidney disease (ADPKD), urinary protein excretion is usually <1 g every 24 hour [1], and renal function declines at a slow rate, i.e., a -2.8 mL/(minute x 1.73 m²) decrease in glomerular filtration rate [2]. In cases of nephrotic-ranged proteinuria and rapid aggravation of renal function, performing a renal biopsy is critical because the other glomerular diseases might be superimposed on ADPKD [3]. We report on a patient with ADPKD who presented with acutely aggravated renal dysfunction and nephrotic-ranged proteinuria. The patient underwent laparoscopic renal biopsy and was properly treated according to the histologic diagnosis.

Case report

A woman 48 year of age visited our hospital for generalized edema and arthralgia in September 2002. She had a family history of hypertension and diabetes mellitus. She had been diagnosed with hypertension, diabetes mellitus, and ADPKD in 2000. She developed swelling in multiple hand joints, arthralgia, and generalized edema in July 2002. Hematologic tests at a local clinic showed the following results: hemoglobin level, 7.4 g/L; total leukocyte count, 4,780/µL; platelet count, 125 x 10³/µL; erythrocyte sedimentation rate 130 mm/hour; C-reactive protein, 0.3 mg/dL; blood urea nitrogen, 44 mg/dL; serum creatinine, 1.7 mg/dL; and 24-hour urine protein, 5,960 mg/day. She was referred to our hospital for further evaluation.

Physical examination showed that her blood pressure was 120/80 mmHg and pulse rate was 80 beats/minute. Both the kidneys were palpable, and bilateral pretilial pitting edema was observed. The laboratory test results were as follows: hemoglobin level, 7.4 g/L; total leukocyte count, 4,780/µL; platelet count, 125 x 10³/µL; erythrocyte sedimentation rate 130 mm/hour; C-reactive protein, 0.3 mg/dL; blood urea nitrogen, 59 mg/dL; creatinine, 2.3 mg/dL; albumin, 2.4 g/dL; total cholesterol, 176 mg/dL; and normal liver enzymes levels. Urinalysis showed 2+ albumin via the dipstick test, >100 red blood cells, and 20–29 leukocytes per high-power field via microscopy. Further investigations showed positive results for antinuclear antibody (ANA; 1:320, homogenous pattern), an anti-dsDNA antibody titre of 857 IU/mL (normal range, <25 IU/mL), and complement C₃ of 22 mg/dL (83–177 mg/dL) and <5 mg/dL (16–47 mg/dL).
respectively. Abdominal ultrasonography showed multiple cysts in the liver and in both kidneys. The right and left kidneys were 18 cm and 19 cm in length, respectively, and the largest cyst was 6.2 cm in the left. Computed tomography (CT) confirmed the ultrasound result and diagnosis of ADPKD (Fig. 1).

The patient’s history of arthritis, overt proteinuria, high anti-dsDNA antibody titer, and positive ANA results satisfied the systemic lupus erythematosus criteria. Her creatinine level, which was 1.7 mg/dL at 3 weeks before visiting our hospital, rapidly increased to 2.4 mg/dL; therefore, we decided to perform a renal biopsy.

A laparoscopic renal biopsy was performed in the right kidney without complication. Light microscopy showed (Fig. 2) 20 glomeruli in the biopsy sample, of which five (25%) exhibited global sclerosis; one exhibited (5%) segmental sclerosis; and 13 exhibited (65%) crescent formation. During immunofluorescence analysis, the glomeruli showed diffuse granular peripheral staining of immunoglobulin (Ig) G, IgA, C3, and C1q. Electron microscopic analysis (Fig. 2) showed many subepithelial and some mesangial electron-dense deposits. The glomerular basement membrane was irregularly thick, and the epithelial foot processes showed marked effacement. Collectively, these observations were consistent with those for diffuse proliferative lupus nephritis [LN; World Health Organization (WHO) Class IV].

After the patient underwent empirical methylprednisolone pulse therapy, 1 g per day for 3 days, she was put on intravenous cyclophosphamide pulse therapy, 500 mg monthly, and oral corticosteroid therapy. The cyclophosphamide pulse therapy continued for 8 months, i.e., up to May 2003, and the serum creatinine levels decreased to 1.5 mg/dL. Subsequently, an additional four cycles of cyclophosphamide pulse therapy were administered every 2 or 3 months; because the proteinuria levels increased again, seven additional cycles were administered until May 2006. Although, no elevation in autoantibody titers and extra-renal lupus manifestation was observed, the patient’s renal function gradually declined over the years (Fig. 3). In October 2010, she developed uremic symptoms and orthopnea because of volume overload; therefore, hemodialysis was started. Currently, she is undergoing regular hemodialysis.

### Discussion

This is a rare case of LN proved in a patient with ADPKD who presented with nephrotic-ranged proteinuria. To our knowledge, this patient represents the first case wherein a biopsy was performed for an ADPKD patient by using a laparoscopic procedure.

Proteinuria is frequently detected in ADPKD patients [1], but nephrotic-ranged proteinuria is unusual. The presence of nephrotic-ranged proteinuria in ADPKD has been reported in 21 cases among the English literatures so far. Various histologic subtypes that have been described in the literature are summarized in Table 1. The two main diseases with regard to superimposition of ADPKD are focal segmental glomerulosclerosis (5/21, 23.8%) and membranous nephropathy (4/21, 19.0%). LN is very rare in patients with ADPKD, and this index case is the third reported case. As other secondary glomerular diseases might superimpose on ADPKD, a biopsy should be considered when unusual manifestations such as nephrotic-ranged proteinuria are detected.

Although renal biopsy is important, multiple bilateral cysts in ADPKD are assumed to be a relative contraindication for percutaneous renal biopsy because of the presumed risk of complications and difficulties involved in obtaining tissue suitable for diagnosis [4]. D’Cruz and colleagues [5] previously described a patient with ADPKD biopsied by open surgical procedure and mentioned that nephrologists are reluctant to perform renal biopsy in patients with ADPKD because this usually entails an open renal biopsy. In the literatures, among the 21 biopsied ADPKD cases, only five cases were performed by percutaneous

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**Figure 1.** Abdominal CT reveals multiple cysts in both kidneys. CT, computed tomography.

**Figure 2.** Renal histopathology. (A) Light microscopy image shows a glomerulus with mesangial hypercellularity and neutrophilic infiltration (periodic acid-Schiff stain × 400). (B) Electron microscopy image shows many subepithelial and some mesangial electron-dense deposits (× 6000).
A renal biopsy under direct vision may be preferred, and an open renal biopsy is performed in most cases of polycystic kidney disease that need a biopsy [3, 5–7]. However, with advances in endoscopic instrumentation, the development in laparoscopic renal biopsy now provides a minimally invasive alternative to open renal biopsy [6,8]. The laparoscopic approach to kidney biopsy offers many advantages, including sufficient diagnostic sample, minimal injury risk, hemostasis under direct vision, a smaller incision, and a short hospital stay [9,10]. We performed the laparoscopic renal biopsy without complication and obtained tissue suitable for analysis.

In summary, our case emphasizes the need to perform renal biopsy in patients with ADPKD and nephrotic-ranged proteinuria for precise diagnosis and proper management. The laparoscopic approach for kidney biopsy was found to be safe and reliable; therefore, we suggest this method for diagnosis in similar cases.

**Conflict of interest**

No conflict of interest.

**References**

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**Table 1. Renal histology in cases with nephrotic-ranged proteinuria in ADPKD patients reported in the literature**

| Number | Histopathology                        | Renal biopsy          | Reference         |
|--------|---------------------------------------|-----------------------|-------------------|
| 1      | Focal glomerulosclerosis              | Open                  | Murphy, 1990      |
| 2      | Focal glomerulosclerosis              | Open                  | Montoyo, 1992     |
| 3      | Focal glomerulosclerosis              | Open                  | Dionisio, 1993    |
| 4      | Focal glomerulosclerosis              | Open                  | Contreas, 1995    |
| 5      | Focal glomerulosclerosis              | Open                  | Savaj, 2012       |
| 6      | Membranous glomerulonephropathy       | Open                  | Shikata, 1991     |
| 7      | Membranous glomerulonephropathy       | Unknown               | Saxena, 1993      |
| 8      | Membranous glomerulonephropathy       | Percutaneous          | Kengne-wafo, 2010 |
| 9      | Membranous glomerulonephropathy       | Percutaneous          | Peces, 2011       |
| 10     | Minimal change disease                | Percutaneous          | Nakahama, 1991    |
| 11     | Minimal change disease                | Open                  | Kuroki, 1995      |
| 12     | Immunoglobulin A nephropathy          | Open                  | Panisello, 1988   |
| 13     | Immunoglobulin A nephropathy          | Open                  | Hiura, 2006       |
| 14     | Crescentic glomerulonephritis         | Open                  | Lucina, 1981      |
| 15     | Intercapillary diabetic glomerulosclerosis | Percutaneous        | Hariharan, 1987  |
| 16     | Type 1 membranoproliferative glomerulonephritis | Open          | Villar, 1992      |
| 17     | Mesangiproliferative glomerulonephritis | Open                | Villar, 1992      |
| 18     | Mesangiproliferative glomerulonephritis | Unknown             | Seyrek, 1995      |
| 19     | Amyloidosis                           | Gingiva, rectum biopsy only | Sar, 2007       |
| 20     | Diffuse proliferative glomerulonephritis | Open              | D’Cruz, 2010      |
| 21     | Class V, lupus nephritis              | Percutaneous          | Wan, 2009         |
| 22     | Class IV, lupus nephritis             | Laparoscopic          | Index case        |

ADPKD, autosomal dominant polycystic kidney disease.
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