Kidney transplant patient with immunoglobulin A nephropathy subsequently diagnosed as concurrent autosomal dominant polycystic kidney disease during 17-year follow-up

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Abstract

A 14-year-old Japanese boy was diagnosed with immunoglobulin A nephropathy resulting in end-stage kidney disease (ESKD). He underwent ABO-compatible living kidney transplantation from his father at the age of 27. In the process of selecting a donor before the transplantation, it turned out that his mother had polycystic kidneys and that her family had a history of hypertension and cerebrovascular diseases. The patient himself also had bilateral multiple kidney cysts, with a normal-sized kidney, confusing us to make the diagnosis of acquired cystic kidney disease (ACKD) or ADPKD difficult at that point. Seventeen years later, his native kidneys showed bilateral swelling with multiple cysts. This, along with the histories of his mother and her relatives and with the existence of multiple liver cysts, led us to confirm the diagnosis of autosomal dominant polycystic kidney disease, not of ACKD. Contrary to previous studies that have suggested the size of cysts both in ADPKD and ACKD reduced with time, the present case showed an increase of 3.0% per year in total kidney volume (TKV) by computed tomography. It suggested the possibility that TKV, after decreasing in the relatively early stage after transplantation, may later increase in the long term after ESKD due to another kidney injury.

Keywords Kidney transplantation · Autosomal dominant polycystic kidney disease · Total kidney volume · Immunoglobulin A nephropathy · End-stage kidney disease

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a heritable kidney disease characterized by the development of multiple cysts in both kidneys and extra-renal organ manifestations such as liver and pancreatic cysts and cerebral aneurysms and can be a recipient for kidney transplantation [1]. It generally shows increased total kidney volume (TKV),

but previous reports have indicated that TKV decreased in the early phase after kidney transplantation [2–4]. We report a rare case of a kidney transplant patient with immunoglobulin A (IgA) nephropathy, subsequently diagnosed as concurrent ADPKD with increased TKV during 17 years of follow-up. Additionally, we discuss concurrent glomerulonephritis in patients with ADPKD.

Case report

The patient presented with proteinuria at the age of 11 and was diagnosed with immunoglobulin A (IgA) nephropathy via renal biopsy at the age of 14. At the diagnosis of IgA nephropathy, the existence of kidney and liver cysts was unknown. At the age of 26, his renal function finally resulted in end-stage kidney disease (ESKD) requiring maintenance hemodialysis. As he hoped to receive a living kidney transplant, his parents received a medical checkup as candidate donors. The checkup revealed that his mother

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had polycystic kidneys without renal insufficiency and that her relatives had a history of hypertension and cerebrovascular diseases, but not dialysis patients. The patient himself also had bilateral multiple kidney cysts and liver cysts, with a normal-sized kidney, making the diagnosis of acquired cystic kidney disease (ACKD) or ADPKD difficult. At the transplantation, the information of precise measurement in both TKV was unknown. Moreover, the genetic examination for definitive diagnosis was not done. After 1 year, at the age of 27, he underwent ABO-compatible living kidney transplantation from his father and he took immunosuppressants, cyclosporine A (CsA), azathioprine (Aza), and prednisolone. His graft function remained stable, with serum creatinine 1.0 to 1.2 mg/dL thereafter with CsA and AZA. He underwent a 10-year protocol biopsy at the age of 37, without presenting any findings of rejection or recurrence of IgA nephropathy. At this time, the routine abdominal ultrasound was performed, but the volume of both kidneys was not measured on computed tomography (CT). He continued follow-up visits every 2 months and at the age of 44, in a routine checkup by abdominal ultrasound, his native kidneys were found to be bilaterally swelling with multiple cysts and multiple liver cysts were confirmed. We reviewed previous medical records and believed to diagnose ADPKD, rather than ACKD based on clinical practice guideline for ADPKD [5]. At this time, estimated glomerular filtration rate (eGFR) was 52.3 mL/min/1.73 m² and urinary abnormality was not seen. CT suggested ADPKD with TKV of 352 mL, led us to confirm the diagnosis of ADPKD, while comprehensively considering his family history and clinical course (Fig. 1a). The past measurement of TKV has never been confirmed. A follow-up CT after 2 years showed an increase in TKV from 352 to 376 mL (a 3.0% per year increase), suggesting the diagnostic accuracy of ADPKD in this recipient (Fig. 1b). Currently, his renal function at the age of 49 showed 53.5 mL/min/1.73 m² of eGFR without urinary abnormalities.

Discussion

We report a case of a kidney transplant patient with IgA nephropathy subsequently diagnosed as concurrent ADPKD during long-term follow-up. Here we mention the diagnosis of ADPKD differentiated from ACKD, post-transplant TKV in ADPKD, and the concurrent glomerulonephritis associated with ADPKD.

When diagnosing ADPKD, the disease should be differentiated from other renal cystic diseases, including ACKD, multiple simple renal cyst, autosomal recessive polycystic kidney disease (ARPKD), and tuberous sclerosis complex. Especially, ACKD, exists in 7% of chronic kidney disease and 20% of ESKD patients, is often confused with ADPKD

Fig. 1 Bilateral native kidney in computed tomography at age 44 (a) and at 46 (b). Total kidney volume was 352 mL (a) and 376 mL (b), respectively

[6]. Even though mutations in *PKD1* and *PKD2* have been known as the causative agents in ADPKD, genetic diagnosis is not common worldwide, usually making a diagnosis with a family history and findings in image inspection, including CT. The most notable difference between ADPKD and ACKD is the size of the kidneys, showing the renal atrophy in ACKD, whereas the swelling in ADPKD with time [7]. In transplanted kidneys, however, the size of cysts usually reduces with time in both ADPKD and ACKD, making diagnosis more difficult. The present case was diagnosed as ADPKD, taking into account an enlargement of the native kidneys, the histories of his mother and her relatives and hepatic cyst formation of extra-renal manifestation.

Several previous reports on post-transplant ADPKD have indicated that TKV was reduced after kidney transplantation. In 1985, Thaysen et al. [2] first reported a TKV reduction of 0.28% per month after transplantation. Yamamoto et al. [3] mentioned TKV decreases of $37.3 \pm 17.9\%$ 1 year after transplantation, $40.6 \pm 18.1\%$ over 3 years, and $32.6 \pm 10.9\%$ over 5 years. Jung et al. [4] described that TKV decreased by 20.2% after 0.5–1 year, 28.6% in 1–3 years, 38.3% in

3–10 years, and 45.8% in more than 10 years. They suggested that TKV decreased rapidly within the first year after transplantation and decreased slowly afterward. The reduction of blood flow due to calcineurin inhibitor has been considered a possible cause of TKV decrease, but this has not been confirmed and the cause of the reduction has remained unclear [3, 4]. These previous reports were focused mainly on the duration of the post-transplant period within 10 years and they differed from the present case of 17 years of follow-up after kidney transplantation. The present findings may suggest that TKV is able to increase after reaching a limit of TKV reduction.

As for post-transplant ACKD, different from the present case, Ishikawa et al. reported that cysts in ACKD usually showed regression after kidney transplantation [8]. Among the seven cases, two cases showed decrease in the size of the native kidneys, three cases had few or no cysts after transplantation, and the remaining cases were one case with incomplete disappearance of cysts and one case with the increase in the number of cysts. Although the size change with long-term follow-up was unknown, the native kidneys of almost patients with ACKD seemed to lose their volumes.

Finally, we describe 29 previously reported cases of ADPKD with concurrent glomerulonephritis, including concurrent focal segmental glomerulosclerosis, minimal change nephritic syndrome, and membranous nephropathy [9]. Among these 29 cases, two were cases with IgA nephropathy that developed during the course of ADPKD. One was a case of a 67-year-old female with serum creatinine 6.3 mg/dL at referral and the other was a case of a 70-year-old male with serum creatinine 1.7 mg/dL at referral [10, 11]. Both of these patients received an open kidney biopsy leading to the diagnosis of IgA nephropathy many years after the diagnosis of ADPKD. This was a different course from the present case, in which IgA nephropathy was identified first, followed by the recognition of ADPKD afterward.

We presented a case of post-kidney transplantation for IgA nephropathy, in which we finally reached a definitive diagnosis of ADPKD after long-term follow-up. Post-transplant TKV in ADPKD has been known to decrease within 10 years after transplantation, but the present case suggested the possibility that TKV later begins to increase in the long run after transplantation. The further cohort study dealing with long-term temporal change of TKV in post-transplant patients with ADPKD was desirable for elucidation of the present issue.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Informed consent about clinical practice was obtained from the patient included in the case report.

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