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Case Presentation

A Case of Good Efficacy of Tolvaptan in a Patient with Markedly Enlarged Polycystic Kidney

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Abstract

A 61-year-old patient with autosomal dominant polycystic kidney disease (Irazabal class 1E) in whom renal function had decreased and kidney size had increased over the past 3 years (change in serum creatinine, 1.3 mg/dL to 1.5 mg/dL; change in total kidney volume, 5632 cm^3 to 7301 cm^3) was treated with tolvaptan 60 mg/day. After 8 years of tolvaptan treatment, serum creatinine remained at 1.51 mg/dL, and total kidney volume was at 6812 cm^3. Adequate salt intake and good weight control may have resulted in good outcomes, even in patients with treatment-resistant giant cystic kidney disease.

More Information

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Keywords: Autosomal Dominant Polycystic Kidney Disease (ADPKD); Polycystic kidney

Introduction

In patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD), kidney size increases over time and renal function progressively declines [1]. The vasopressin V2 receptor antagonist tolvaptan is used worldwide to slow these developments in such patients [2]. In patients with larger kidneys, the progression of renal function decline is more rapid, but the therapeutic effect of tolvaptan is poorer in such patients [3]. We report on a man with ADPKD with a history of large kidneys and progressive renal decline in whom kidney size and renal function have been well controlled for 8 years with tolvaptan.

Case report

A 61-year-old man was admitted to our hospital with abdominal fullness and progressive renal impairment. ADPKD and hypertension had been diagnosed at the age of 50 years during a medical check-up. At age 58 years, the total kidney volume (TKV) of both kidneys was 5632 cm^3 (calculated from computed tomography [CT] images by synapse Vincent software) [4], serum creatinine was 1.3 mg/dL, and estimated glomerular filtration rate (eGFR) was 50.0 ml/min/1.73 m^2. Treatment with 20 mg/day olmesartan (an angiotensin II receptor antagonist), and 40 mg/day nifedipine (a calcium antagonist) had been administered for hypertensive treatment for 10 years.

On admission, the patient was 166 cm tall and weighed 72.2 kg. His blood pressure was 110/76 mm Hg, and his body temperature was 36.5 °C. Heart and breath sounds were normal. He had significant abdominal distention and edema in the extremities. Laboratory findings were as follows: total protein, 6.1 g/dL; albumin, 3.1 g/dL; serum creatinine, 1.49 mg/dL; and eGFR, 38.5 ml/min/1.73 m^2. The 24-hour urinary protein excretion was 0.05 g, and the urine sediment contained less than one red cell per high-power field. CT showed marked enlargement of both kidneys and numerous renal cysts. The TKV of both kidneys was 7301 cm^3. The liver was elevated by the enlarged kidneys, and numerous small cysts were also present in the liver; however, hepatomegaly was not evident (Figure 1).

Magnetic resonance imaging showed a cerebral aneurysm in the M1 region of the left middle cerebral artery.

Although no family members had presented with the same disease, genetic analysis showed a heterozygous missense mutation in PKD1, the gene responsible for ADPKD:

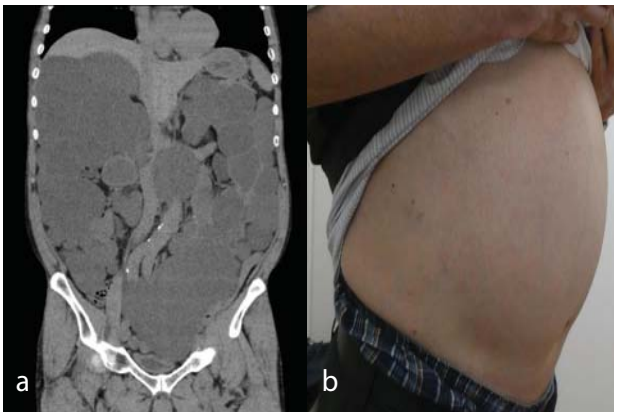

Figure 1: Maging findings.
a: Computed tomography coronary image showing an enlarged kidney.
b: Gross image showing abdominal distension due to the enlarged kidneys.

PKD1 (NM_001009944.2): c.5770G>A: p.Gly1924Ser: heterozygous.

Tolvaptan (a vasopressin V2 receptor antagonist) was initiated at a dose of 60 mg/day.

Clinical course

After starting treatment, the patient's body weight decreased from 72 kg to 69 kg, and the associated edema in the lower legs disappeared due to increased urine output. After 1 year, no adverse effects of tolvaptan on the patient's living environment were observed, the dose of tolvaptan was increased to 90 mg/day, and after 2 years, it was increased again to 120 mg /day; thereafter, the patient continued at this dose. Eight years later, the patient's body weight was 68 kg, and renal function and TKV were stable (eGFR, 34 ml/min/1.73 m^2; TKV, 6812 cm^3) (Figure 2). The patient's salt intake over 8 years was calculated to be 6 to 7 g/day.

Discussion

We presented the case of a 61-year-old man with ADPKD in whom tolvaptan prevented further changes in kidney size and function.

Torres, et al. first reported in 2012 that in patients with ADPKD, tolvaptan is effective at reducing the rate at which kidney size increases and renal function declines [2]. However, although they showed an overall statistical advantage of tolvaptan over placebo, the variability of the effect was large and some patients showed no effect.

Irazabal, et al. examined the natural course of ADPKD over time and classified patients according to kidney size; they found that the larger the kidneys, the faster the progression of renal function decline [3]. They also investigated the effect of tolvaptan on kidney size and showed that tolvaptan was more effective than placebo in slowing the progression of renal function decline in all kidney size classes; however, renal function declined also in the tolvaptan group, and the decline was faster in the group with larger kidneys [5].

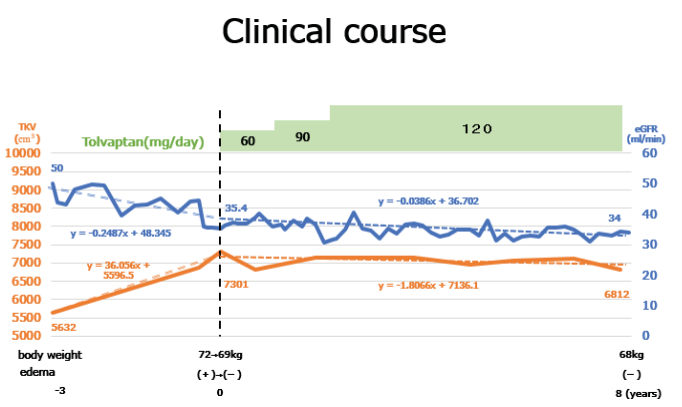

Figure 2: Clinical course. Progressive decline in renal function and increase in total kidney volume during the 3 years before tolvaptan administration. Tolvaptan treatment prevented further renal function decline and increase in total kidney volume for 8 years. TKV, total kidney volume.

Horie, et al. reported the effect of three years of tolvaptan treatment in patients in Japan and found similar results, i.e., steady progression of renal function decline and poor renal prognosis, especially in patients with large kidneys [6]. Other authors reported similar findings but did not provide further information [7-9]. Chebib, et al. suggested that tolvaptan showed poor efficacy because it was administered to patients with progressive renal impairment and that it might show better efficacy in patients with better renal function [10].

To date, no studies have compared characteristics of patients in whom tolvaptan does or does not show efficacy. Because tolvaptan is a diuretic, patients are instructed to drink plenty of water. However, in our experience, patients who drink a lot of water have excessive salt intake, which in turn leads to overeating. Consequently, we have observed weight gain in many of our patients; however, the parameter of body weight has not been addressed in previous studies to determine the efficacy of tolvaptan. Based on previous reports and our own experience, we expected the present patient, who was Irazabal class 1E, to have a poor renal prognosis and a poor response to tolvaptan. However, the patient was doing well after 8 years of treatment with tolvaptan. Therefore, we suggest that tolvaptan has been effective in this patient because he did not gain weight during the treatment period and controlled his salt intake appropriately.

Conclusion

Tolvaptan has a strong diuretic effect, so patients are instructed to drink large amounts of water. However, drinking a lot of water may lead to weight gain, which reduces the efficacy of tolvaptan in suppressing the progression of renal function decline. We propose this concept based on our experience with the present patient with ADPKD and large kidneys: The patient had appropriate weight control and salt intake during tolvaptan intake and responded well to tolvaptan, even though a patient with large kidneys would normally be expected to have a weak response to this drug.

Statement of ethics

The present report was produced in conformity with the Declaration of Helsinki, and the patient gave his written consent for this case report to be published.

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