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【 CASE REPORT 】

Repetitive Refractory Renal Cyst Infection in Autosomal Dominant Polycystic Kidney Disease for which Renal Transcatheter Arterial Embolization Was Effective in Preventing Recurrence

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Abstract:

Renal cyst infection is a frequent and serious complication of autosomal dominant polycystic kidney disease (ADPKD) that is often difficult to treat and can be fatal. While nephrectomy is the standard therapy for severe refractory renal cyst infection, it can be associated with severe adverse events. We experienced a case of repetitive renal cyst infection in a 58-year-old Japanese man with ADPKD on dialysis. He underwent renal transcatheter arterial embolization (TAE) four months after the last episodes of renal cyst infection, and his renal cyst infection has not recurred since renal TAE. This case suggested that renal TAE is effective for preventing repetitive renal cyst infection.

Key words: ADPKD, polycystic kidney disease, cyst infection, infected cyst, renal transcatheter arterial embolization

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a common inherited renal disorder (1, 2), and renal or hepatic cyst infection is a frequent and serious complication of ADPKD. It has been estimated that 30% to 50% of patients with ADPKD experience some form of renal infection during their lifetime (3, 4), although cyst infection leading to hospitalization is much less frequent, occurring in approximately 9% of cases (5). These infections sometimes become resistant and can be fatal, even when appropriate antibiotics are administered (5-7). However, much is still unknown about cyst infection in ADPKD.

The most common causative bacteria of cyst infection are reported to be enterobacteria (5, 6, 8). We previously found that cyst infection due to retrograde infection was rare, and hematogenous spread via bacterial translocation in the intestine was considered the main route of cyst infection. We also reported that renal cyst infection may be unlikely to occur after renal transcatheter arterial embolization (TAE) because hematogenous spread via the renal arteries may be prevented by shutting down the renal blood flow. However, in this our previous report, we have just reported the lower frequency of renal cyst infection after renal TAE and we have never reported cases in which renal TAE prevented obvious repetitive renal cyst infection. Whether or not renal TAE can prevent renal cyst infection is still unclear because it is often difficult to specify the cause of fever in patients with ADPKD.

We herein report a case of ADPKD with obvious repetitive renal cyst infection in which renal cyst infection no longer occurred following renal TAE. This is the first case showing the efficacy of renal TAE for preventing renal cyst infection in a patient with definite renal cyst infection.

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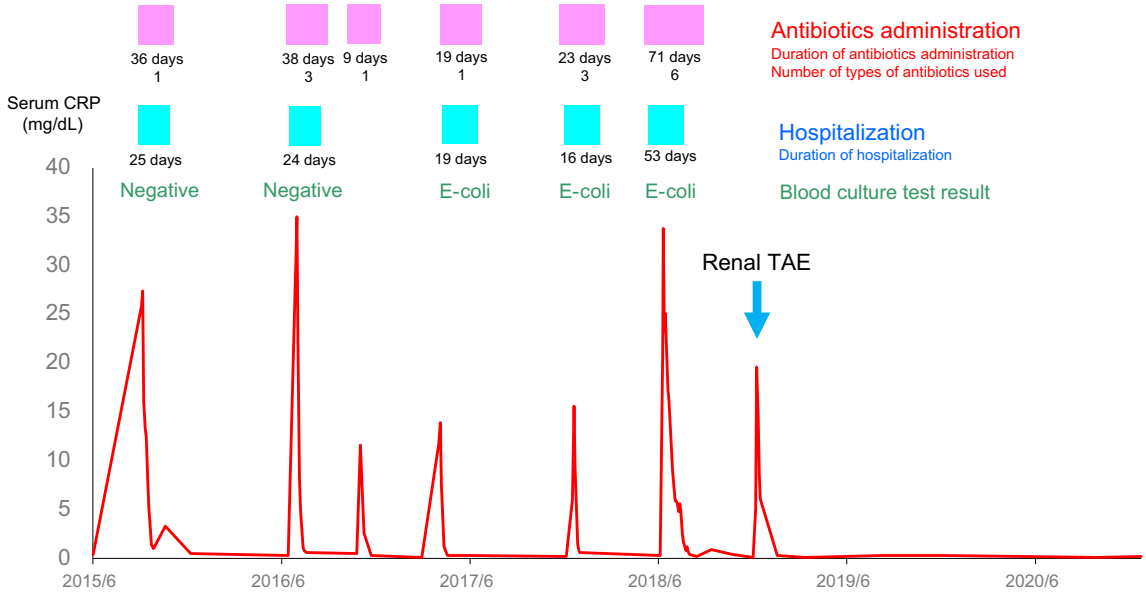

Figure 1. **The clinical course (serum CRP level), use of antibiotics, and duration of hospitalization.**

Table. **Results of the Blood Culture Test at Admission.**

Antibiotics	MIC (μg/mL)	SIR
Ampicillin	≤8	Susceptible
Cefazolin	≤2	Susceptible
Cefepime	≤2	Susceptible
Cefotaxime	≤1	Susceptible
Flomoxef	≤8	Susceptible
Gentamicin	≤2	Susceptible
Levofloxacin	≤0.12	Susceptible
Meropenem	≤0.25	Susceptible
Sulfamethoxazole/trimethoprim	≤2	Susceptible
Tazobactam/piperacillin	≤8	Susceptible

Identified: *Escherichia coli*

MIC: minimum inhibitory concentration, SIR: S (Susceptible) I (Intermediate) R (Resistant)

Case Report

We encountered a 58-year-old Japanese man with ADPKD on dialysis for 14 years who had no other specific medical history. He had a long dialysis history and was completely anuric. He had been hospitalized in our hospital four times due to a diagnosis of left renal infection in the last four years (Fig. 1). He had another episode of suspected cyst infection, though he was not hospitalized at that time.

In 2019, he suddenly had right lower abdominal pain and a fever over 39℃. He was referred to our hospital the same day and admitted. His body temperature was 39.2℃, and he had right lower abdominal pain at admission. His serum C-reactive protein (CRP) level was 21.4 mg/dL, and his white blood cell count was 10,600/μL. Two sets of blood culture tests at admission revealed *Escherichia coli*. The susceptibility of *Escherichia coli* to antibiotics is presented in Table. His blood culture test was positive in two of the other five episodes (Fig. 1).

Imaging examinations

Abdominal computed tomography (CT) was performed as reported previously (9, 10). For magnetic resonance imaging (MRI), transverse and sagittal T1-weighted imaging (T1WI), T2-weighted imaging (T2WI), and diffusion-weighted imaging (DWI) were conducted, as reported previously (9, 10). We evaluated the infected renal cyst according to our diagnostic criteria (9, 10) (Supplementary material). The cyst showed an intracystic fluid-fluid level and a higher intensity on DWI and T1WI than normal cysts (Fig. 2) as well as wall thickening with prominent calcification on CT.

Treatment at the hospital

This case was not considered to have a severe cyst infection on admission, so we did not select fluoroquinolones as first-line antibiotics according to our antibiotic strategy (11). Intravenous antibiotics (cefmetazole sodium 1 g/day) were started just after admission to our hospital (Fig. 3). Cefmetazole was susceptible to *Escherichia coli* cultured from blood culture test *in vitro* (Table). However, his symptoms did not improve sufficiently in response to this treatment, so we considered this case to be refractory cyst infection. Therefore, we added the intravenous administration of levofloxacin (500 mg per hemodialysis) at Day 6 which was also susceptible to *Escherichia coli* cultured from blood culture test *in vitro*. However, his fever remained, so we switched cefmetazole to meropenem (0.5 g/day) at Day 13. His symptoms improved temporarily after switching to meropenem but then worsened again. Therefore, meropenem was switched to flomoxef (1 g/day) at Day 36. After that, his symptoms improved dramatically, and he was discharged from the hospital after 16 days on Day 52. The administra-

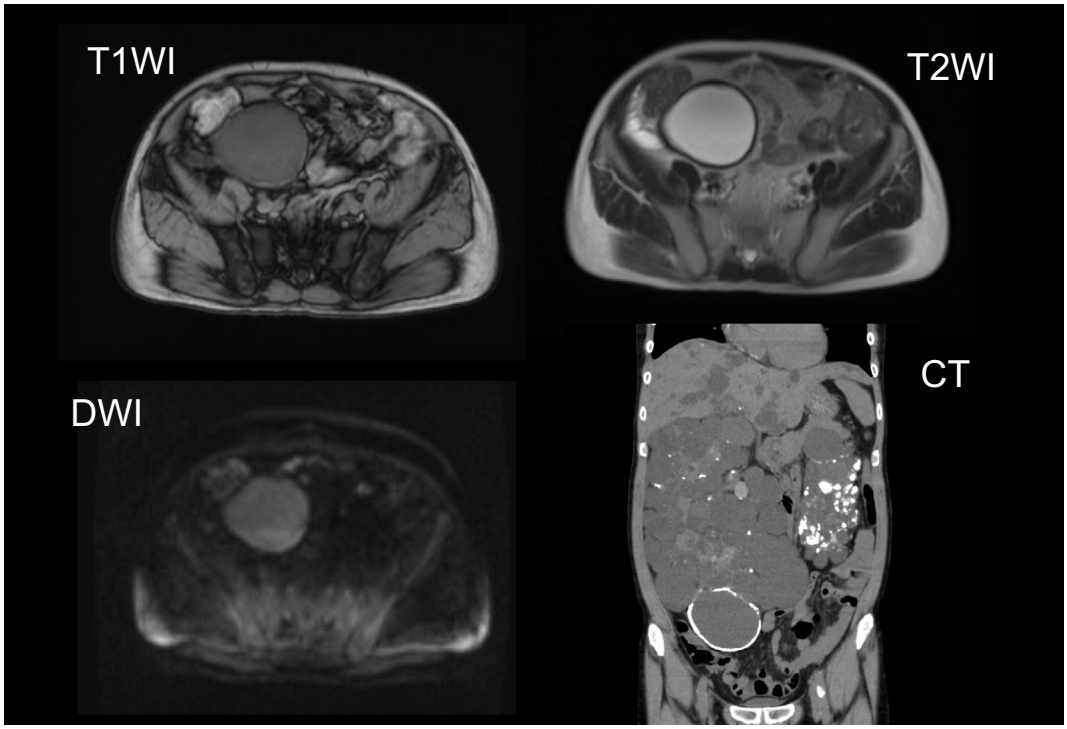

Figure 2. **CT and MRI findings (T1WI, T2WI, and DWI) in the present case. The infected renal cyst shows a higher intensity on DWI and T1WI than normal cysts. Cyst wall thickening with calcification is seen on CT.**

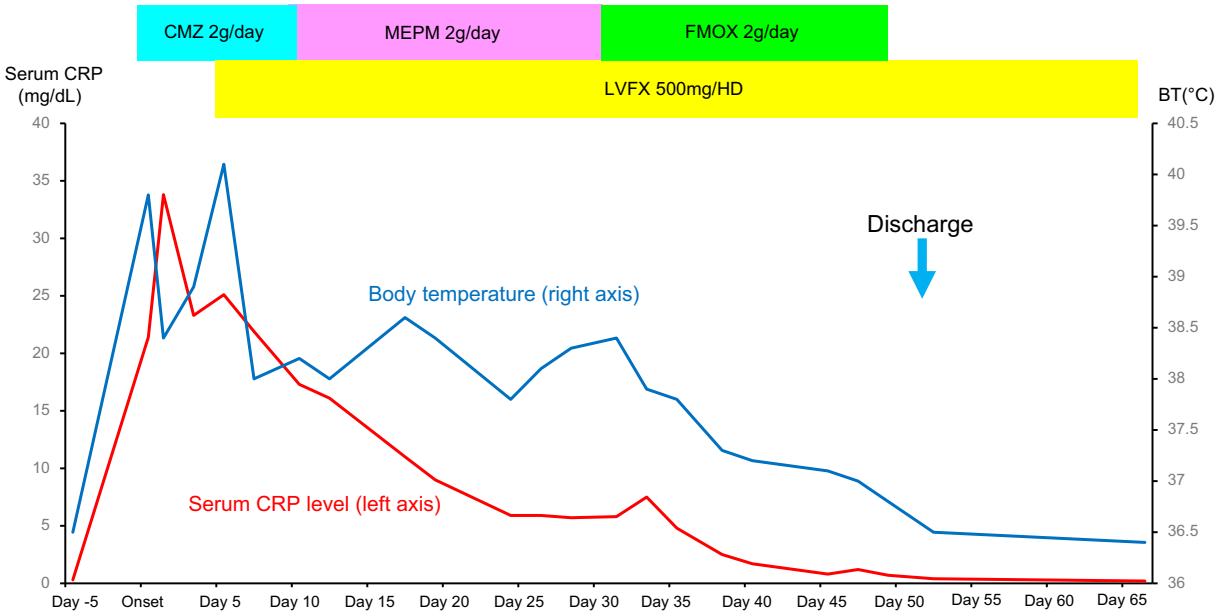

Figure 3. **The clinical course (body temperature and serum CRP level) and use of antibiotics. CMZ: cefmetazole, LVFX: levofloxacin, MEPM: meropenem, FMOX: flomoxef**

tion of levofloxacin was continued for 15 days after his discharge because we considered that it was better to administer antibiotics for approximately 2 weeks after the patient's body temperature was normalized in order to prevent recurrence of cyst infection.

The infected renal cyst was large (diameter: 6 cm), and this episode was the fifth in 4 years, so we considered cyst drainage advisable. However, his infected renal cyst was in the lower pole of the right kidney and could not be drained due to its location (Fig. 2).

Renal TAE

The patient developed recurrent refractory renal cyst infection, and his infected renal cyst was unable to be drained due to its location. We decided to perform renal TAE when he had no symptoms of cyst infection at four months after

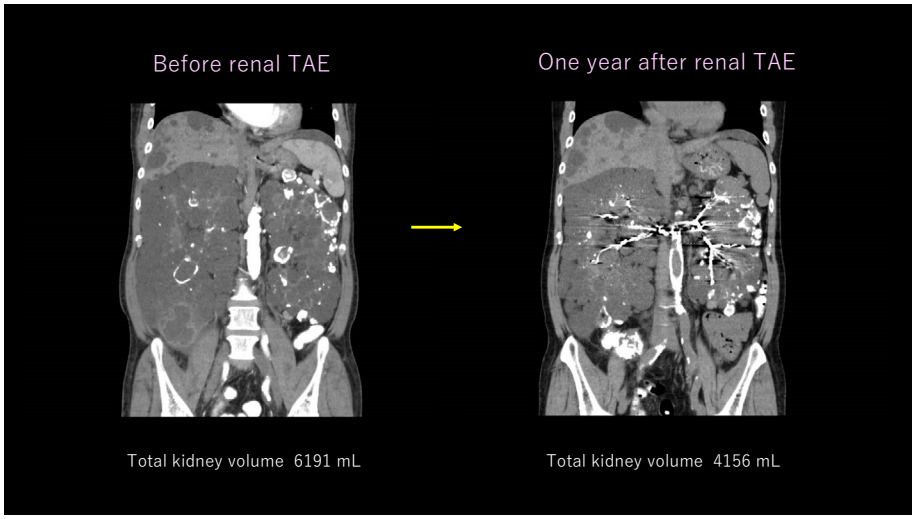

Figure 4. **The CT findings before and one year after renal TAE.**

the last episode of renal cyst infection. In total, 20 microcoils were inserted into his kidneys (Fig. 4). We performed renal TAE as previously reported for the bilateral kidneys (12). We usually perform renal TAE for the bilateral kidneys simultaneously because high blood flow in the remaining artery increases the risk of hemorrhage due to volume overload. To avoid recanalization, coils were inserted as peripherally as possible into small renal artery branches, and both peripheral and proximal renal artery occlusion were performed as completely as possible. Since undergoing renal TAE, he has not suffered from renal cyst infection for more than two years.

Discussion

We reported a case of ADPKD with repetitive renal cyst infection in a patient whose renal cyst infection was obvious by a positive blood test, right lower abdominal pain, and renal imaging consistent with his abdominal pain.

Two findings were notable with this case. The first was that cefmetazole, levofloxacin, and meropenem were not effective enough despite all being effective *in vitro*, although flomoxef was effective. As we reported previously, the intracystic penetration of meropenem into infected cysts was poor (13). These antibiotics may not penetrate infected renal cysts with heavily calcified wall thickening, which might be why meropenem was not very effective in this case. It may also be important to consider the drug half-life in serum in addition to the drug susceptibility when selecting antibiotics (11). The time above the minimum inhibitory concentration (MIC) is an important determinant of the activity of β-lactams. To ensure sufficient time above the MIC of antibiotics in infected cysts, the drug half-life may need to be considered, as the intracystic antibiotics concentration may increase and be sustained for a longer duration the longer its serum concentration is sustained. Flomoxef is a water-soluble antibiotic, but it has long drug half-life in the serum in dialysis patients (14), which might be why it was effective in this patient. The second finding was that renal TAE might have prevented recurrence of renal cyst infection in this patient. Theoretically, hematogenous bacterial spread can be prevented by shutting down the renal blood flow by renal TAE (6, 11, 12). This case supported this hypothesis. The rate of positive blood culture tests in patients with cyst infection is approximately 19% (6). However, renal TAE may be recommended for all patients with repeated renal cyst infections who are anuric on dialysis even when they have a negative blood culture test result because hematogenous bacterial spread may be the main cause of cyst infection. This case suggested that bacterial spread via the blood plays an important role in cyst infection, which may be a useful finding for the management of other infectious diseases.

While nephrectomy may be standard therapy for refractory renal cyst infection when cyst drainage is not suitable, it can be associated with severe adverse events in ADPKD patients, especially elderly patients with comorbid conditions (12). Renal TAE is less invasive than nephrectomy, so it is a promising treatment for preventing repetitive renal cyst infection for such patients. However, we experienced cases of severe renal cyst infection that occurred just after renal TAE when renal cyst infection might have still been active (15). The renal blood flow decreases after renal TAE, so antibiotics may be unlikely to reach the infected renal cysts through the blood flow, and the antibiotics concentration in infected cysts may therefore not achieve the level needed in such patients after renal TAE. Thus, renal cyst infection can progress rapidly after renal TAE and should thus not be performed in patients with active cyst infection. We consider it potentially important to perform renal TAE at least one month after the body temperature and inflammatory reaction on blood tests have normalized in patients with cyst infection in order to prevent severe renal cyst infection just after renal TAE. According to our experience, it may be possible to perform renal TAE even if the administration of antibiotics is not discontinued, on the condition that the

body temperature and blood inflammatory marker levels have normalized for at least one month. Nephrectomy should be considered for patients whose body temperature and inflammatory marker levels have not normalized with antibiotic treatment or cyst drainage. Renal TAE should not be performed for patients with uncontrolled cyst infection. Further studies are needed in order to clarify the effectiveness of renal TAE on renal cyst infection and the optimal timing for performing renal TAE.

In conclusion, we experienced a case of ADPKD in which repetitive renal cyst infection has not occurred since renal TAE was performed.

Informed and voluntary consent for publication was obtained from the patient described in the article.

The authors state that they have no Conflict of Interest (COI).

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