Bacteremic kidney cyst infection caused by *Helicobacter cinaedi*

Kenta Ito¹ · Takumi Yamamoto¹ · Haruomi Nishio¹ · Asako Sawaya¹ ·
Masaaki Murakami¹ · Akiko Kitagawa¹ · Yoko Matsuo¹ · Ken Matsuo¹ ·
Satoshi Tanaka¹ · Noriko Mori¹

Received: 5 October 2015 / Accepted: 20 November 2015 / Published online: 10 December 2015
© Japanese Society of Nephrology 2015

Abstract Cyst infection is one of the major complications in patients with autosomal dominant polycystic kidney disease (ADPKD). The causative pathogen in kidney cyst infection frequently goes undetected. Although only one case report of kidney cyst infection caused by *Helicobacter cinaedi* (*H. cinaedi*) is published in English literature, it may be an important pathogen in kidney cyst infection. Kidney cyst infection and *H. cinaedi* infection share the common characteristic of tendency to relapse and chronic kidney disease is a major risk factor for *H. cinaedi* infection. Moreover, a long period is required to detect *H. cinaedi* in blood cultures, potentially causing false-negative results. After the identification of *H. cinaedi*, we must carefully select antibiotics and the antibiotic treatment period should be extended to prevent recurrence. Here we present a case of a 58-year-old male with ADPKD who developed bacteremic kidney cyst infection caused by *H. cinaedi*. He was admitted to our hospital because of fever, lower left back pain, vomiting, and feeling of abdominal enlargement. *H. cinaedi* was detected from the blood cultures obtained at admission after 4 days of culture. Antibiotics were administered for 8 weeks after confirming negative blood cultures. There was no evidence of kidney cyst infection relapse at 3 months after treatment completion. Nephrologists should regard *H. cinaedi* as a challenging but important pathogen in kidney cyst infection, particularly when the causative organism is unknown or kidney cyst infection is recurrent.

Keywords *Helicobacter cinaedi* (*H. cinaedi*) · Cyst infection · Bacteremia · Autosomal dominant polycystic kidney disease (ADPKD) · Chronic kidney disease (CKD)

Introduction

Cyst infection is one of the major complications in patients with autosomal dominant polycystic kidney disease (ADPKD) [1]. Identification of the causative pathogens can be challenging and nephrologists are frequently unable to identify the pathogens associated with kidney cyst infection. Specifically, the frequencies of causative pathogen identification in blood and urine cultures from the patients with kidney cyst infection are 8–17 and 33–56 %, respectively [1]. *Escherichia coli* (*E. coli*) is the leading pathogen among cases where the pathogen is identified [1].

Although only one case report of kidney cyst infection caused by *Helicobacter cinaedi* (*H. cinaedi*) has been published in English literature [2], we consider *H. cinaedi* as a potentially important pathogen in kidney cyst infection. This hypothesis is based on several factors. First, the clinical conditions of cyst infection and *H. cinaedi* infection are similar in terms of ease of relapse [3]. Second, one of the major risk factors for *H. cinaedi* infection is chronic kidney disease (CKD) [3, 4]. Third, *H. cinaedi* in blood cultures can be sometimes determined to be negative by error [3]. Fourth, the use of fluoroquinolones, which are often used to treat cyst infection, may fail to effectively treat *H. cinaedi* infection [5]. Finally, long-term antibiotic administration is required to adequately treat *H. cinaedi* infection and prevent recurrence [5]. Here we report a case of bacteremic kidney cyst infection in a patient with ADPKD and discuss the association between kidney cyst infection in patients with ADPKD and *H. cinaedi* infection.

✉ Kenta Ito
pa2.kenta@gmail.com

¹ Department of Nephrology, Shizuoka General Hospital, 4-27-1 Kitaando, Aoi-ku, Shizuoka 420-8527, Japan

Case report

A 58-year-old male was admitted to our hospital because of fever, lower left back pain, vomiting, and feeling of abdominal enlargement for 4 days. He had been diagnosed with CKD caused by ADPKD 22 years earlier, and he had been initiated on hemodialysis 1.5 years earlier. Four days before admission, he developed a low-grade fever. At approximately the same time, his family dog that he had kept for 3 months also appeared ill, displaying a poor appetite and alopecia without digestive symptoms. The following day, he vomited during hemodialysis. Subsequently, his symptoms progressively worsened and he was referred to our hospital.

The patient's past medical history was notable for bilateral inguinal hernia and he had undergone an operation for bilateral inguinal hernioplasty 1 year earlier without complications. He appeared ill when he presented at our hospital. His blood pressure was 184/100 mmHg, heart rate was 78 beats/min, and body temperature was 38.8 °C. On physical examination, a systolic heart murmur (Levine III/VI) was audible at the apex. His abdomen was distended and his lower left back was tender. There was no evidence of skin rash. Initial laboratory and urine analyses showed: white blood cell count, 9800/mm³; differential, 85.4 % neutrophils, 9.5 % monocytes, 3.9 % lymphocytes; hemoglobin level, 9.1 g/dL; platelet count, 287,000/mm³; C-reactive protein (CRP) level, 25.69 mg/dL; 2+ proteinuria; 3+ occult hematuria; urinary Gram stain, no white blood cells or bacteria. An unenhanced computed tomography (CT) scan revealed an area of fatty tissue with increased density around the dorsal side of the left polycystic kidney and the ventral side of the right polycystic kidney (Fig. 1).

Fig. 1 Unenhanced abdominal computed tomography scan revealed an area of fatty tissue with increased density around the dorsal side of the left polycystic kidney

Other findings included an increased density in some kidney cysts and colon diverticula without inflammation.

The patient was admitted with a diagnosis of kidney cyst infection and was initiated on ceftriaxone (2 g daily). On hospital day 4, Gram-negative, spiral-shaped bacteria were detected from the blood cultures that were obtained at admission (Fig. 2). Antibiotic treatment was changed to gentamicin (loading dose 5 mg/kg, maintenance dose 2 mg/kg after dialysis) and ampicillin-sulbactam (3 g daily). On hospital day 6, his loose stool was positive on a *Clostridium difficile* toxin assay and metronidazole (1500 mg daily for 10 days) was added to his treatment. On hospital day 7, the inflammatory findings on CT examination had improved and his feeling of abdominal enlargement had resolved. On hospital day 10, the Gram-negative, spiral-shaped bacteria were identified as *H. cinaedi*. A blood agar plate growth showed a characteristic *H. cinaedi* “thin-spread colony” morphology (Fig. 3). In addition, bacterial identification as *H. cinaedi* was confirmed using matrix-assisted laser desorption/ionization-time of flight mass spectrometry (Bruker Daltonics Inc., Billerica, MA, USA). Follow-up blood cultures obtained on hospital days 2 and 10 and stool cultures obtained on hospital days 6 and 7 did not yield *H. cinaedi* growth, even after an extended culture period to 10 days. Vegetations were also undetectable with transthoracic echocardiography. On hospital day 12, although his fever did not subside, he was discharged to resume his work. His treatment antibiotics were changed to oral minocycline (200 mg daily), oral amoxicillin (500 mg on non-dialysis days), and intravenous ampicillin-sulbactam (3 g post-dialysis). On day 18, his body temperature had further declined and he

Fig. 2 Gram staining of *Helicobacter cinaedi* isolated by aerobic blood culture

discontinued taking antipyretic medications. CRP level also steadily declined. On day 58, antibiotic treatment was discontinued following 8 weeks of confirmed negative blood cultures (Fig. 4).

There was no evidence that the kidney cyst infection had relapsed 3 months after the end of his treatment. We have continued to evaluate him closely without treatment as an outpatient to monitor for potential relapse.

Discussion

We have described a case of bacteremic kidney cyst infection caused by *H. cinaedi* in a patient with ADPKD. The prevalence of ADPKD in Japan is 1:4033 [6]. Among

Fig. 3 Thin spread colony formation was evident on a blood agar plate

patients with ADPKD, cyst infection is responsible for 11 % of all hospital admissions [1]. In particular, kidney cyst infection accounted for 5.4 and 20.6 % of all causes and infection-related causes of death, respectively, in this population [7]. The frequency of positive blood and urine cultures in kidney cyst infection are 8–17 and 33–56 %, respectively [1]. In cases with an identified pathogen, *E. coli* is the most frequently detected pathogen [1]. However, nephrologists are sometimes forced to manage kidney cyst infection without identification of pathogen. This situation can be very troubling. There is only one published case report describing kidney cyst infection caused by *H. cinaedi* in English literature [2]. In a case series on *H. cinaedi* bacteremia, cyst infection or cholangitis were the sources of bacteremia in 5 out of 63 patients [3]. In addition to these clinical reports, there are two judicious issues that suggest a relationship between kidney cyst infection and *H. cinaedi*. First, kidney cyst infection and *H. cinaedi* infection are similar in terms of ease of relapse. Bacteremia caused by *H. cinaedi* recurs in 24 % of cases [3]. Although we could not find published data on the frequency of kidney cyst infection recurrence, nephrologists often treat recurrent kidney cyst infection. Second, CKD is one of the major risk factors for *H. cinaedi* infection. In some reports, one-third of the patients with *H. cinaedi* bacteremia had CKD [3, 4]. Indeed, ADPKD is one of the major causes of CKD in Japan [6]. Considering from these viewpoints, in conjunction with our report, we consider that nephrologists should bear in mind that *H. cinaedi* can be an undetected but important pathogen in kidney cyst infection. Particularly regarding the detection of *H. cinaedi*, there is the possibility that blood cultures might be mistakenly determined to be negative. In the present case,

Fig. 4 Clinical course after admission. *HD* hemodialysis

H. cinaedi was detected in blood cultures, but not until hospital day 4. The reported median culture period to detect *H. cinaedi* from blood is 5 days [3]. If the typical blood culture incubation period is 5 days, as it is at our hospital, 45 % of the cases with bacteremia caused by *H. cinaedi* will be overlooked [3]. Extended blood cultures incubation periods of 7, 10, and 12 days can improve the frequency of *H. cinaedi* detection to 87, 98, and 100 %, respectively [3]. Moreover, we must pay attention to some caveats when treating *H. cinaedi* infection. First, the administration of fluoroquinolones alone may result in a treatment failure when treating *H. cinaedi* infection. Trimethoprim–sulfamethoxazole or fluoroquinolones are often selected to treat cyst infection because of their tendency to penetrate into the cysts [8–10]. Fluoroquinolones are often selected with consideration of the side effects of hyperkalemia induced by trimethoprim–sulfamethoxazole, particularly in patients with CKD. Although there are no general guidelines for the treatment of *H. cinaedi* infection, penicillins, tetracycline, and aminoglycosides are regarded as being more effective than cephalosporins, erythromycin, or ciprofloxacin [5]. Treatment with fluoroquinolone alone is not recommended [5], because *H. cinaedi* in Japan is often resistant to fluoroquinolones because of a point mutation in the bacterial DNA gyrase genes [11]. Second, long-term antibiotic administration is required to adequately treat *H. cinaedi* infection and prevent recurrence. Kidney cyst infection is treated with antibiotics for an average of 5 weeks [1]. However, *H. cinaedi* infection generally require prolonged administration of antibiotics [5] and a single reported case of kidney cyst infection caused by *H. cinaedi* was successfully treated with antibiotics for 9 weeks [2]. In the present case, we administered antibiotics for 8 weeks after confirming that blood cultures negative for a total of 58 days. Three months after the end of treatment, the kidney cyst infection had not recurred. If we manage the frequently relapsing kidney cyst infection without the identification of pathogen, we may try to administer antibiotics for longer periods while worrying about the possibility of *H. cinaedi*.

In conclusion, nephrologists should keep in mind that *H. cinaedi* is an under-recognized but important pathogen in kidney cyst infection, in particular for cases where the causative pathogen is unknown or kidney cyst infection is recurrent. In such situations, the blood culture incubation period should be extended to maximize the chances of

detecting *H. cinaedi*, and the antibiotic treatment period should be extended to prevent recurrence. Further studies are warranted to clarify the association between kidney cyst infection and *H. cinaedi*.

Acknowledgments We appreciate doctors at Johoku Kyoritsu Clinic for administration of antibiotics after hemodialysis. Furthermore, we appreciate clinical microbiology technologists at Shizuoka General Hospital and Chutoen General Medical Center for identification of *H. cinaedi*.

Compliance with ethical standards

Conflict of interest The authors have declared that no conflicts of interest exists.

References

1. Sallée M, Rafat C, Zahar JR, et al. Cyst infections in patients with autosomal dominant polycystic kidney disease. *Clin J Am Soc Nephrol*. 2009;4:1183–9.
2. Mandai S, Kasagi Y, Kusaka K, et al. *Helicobacter cinaedi* kidney cyst infection and bacteremia in a patient with autosomal dominant polycystic kidney disease. *J Infect Chemother*. 2014;20:732–4.
3. Araoka H, Baba M, Kimura M, et al. Clinical characteristics of bacteremia caused by *Helicobacter cinaedi* and time required for blood cultures to become positive. *J Clin Microbiol*. 2014;52:1519–22.
4. Matsumoto T, Goto M, Murakami H, et al. Multicenter study to evaluate bloodstream infection by *Helicobacter cinaedi* in Japan. *J Clin Microbiol*. 2007;45:2853–7.
5. Uçkay I, Garbino J, Dietrich PY, et al. Recurrent bacteremia with *Helicobacter cinaedi*: case report and review of the literature. *BMC Infect Dis*. 2006;6:86–90.
6. Higashihara E, Nutahara K, Kojima M, et al. Prevalence and renal prognosis of diagnosed autosomal dominant polycystic kidney disease in Japan. *Nephron*. 1998;80:421–7.
7. Fick GM, Johnson AM, Hammond WS, et al. Causes of death in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol*. 1995;5:2048–56.
8. Elzinga LW, Golper TA, Rashad AL, et al. Trimethoprim-sulfamethoxazole in cyst fluid from autosomal dominant polycystic kidneys. *Kidney Int*. 1987;32:884–8.
9. Elzinga LW, Golper TA, Rashad AL, et al. Ciprofloxacin activity in cyst fluid from polycystic kidneys. *Antimicrob Agents Chemother*. 1988;32:844–7.
10. Hiyama L, Tang A, Miller LG. Levofloxacin penetration into a renal cyst in a patient with autosomal dominant polycystic kidney disease. *Am J Kidney Dis*. 2006;47:e9–13.
11. Kawamura Y, Tomida J, Morita Y, et al. Clinical and bacteriological characteristics of *Helicobacter cinaedi* infection. *J Infect Chemother*. 2014;20:517–26.