Refractory *Salmonella enterica* Serotype *choleraesuis*-Related Renal Cyst Infection in a Patient with Autosomal Dominant Polycystic Kidney Disease Undergoing Hemodialysis Treated Successfully with Intracystic Ciprofloxacin Infusion

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Key Words

Autosomal dominant polycystic kidney disease • Intracystic ciprofloxacin • Renal cyst infection • *Salmonella enterica* serotype *choleraesuis* bacteremia

Abstract

Objective: To report a potential salvage therapy for refractory renal cyst infection secondary to *Salmonella enterica* serotype *choleraesuis* (*S. choleraesuis*). **Clinical Presentation and Intervention:** A 52-year-old male with autosomal dominant polycystic kidney disease undergoing hemodialysis experienced an episode of *S. choleraesuis*-related gastroenteritis subsequently complicated by bloodstream and refractory renal cyst infection with formation of multiple pyocysts. The patient was treated with intracystic indwelling diluted ciprofloxacin solution. **Conclusion:** In this patient, intracystic infusion of ciprofloxacin achieved a sufficient antibiotic level in infected renal cysts and hence completely eradicated *S. choleraesuis*. Therefore, intracystic antibiotic infusion could be a potential salvage therapy for refractory renal cyst infection.

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Introduction

Nontyphoid *Salmonella* are important foodborne pathogens that cause gastroenteritis, bacteremia and subsequent septic metastases, especially in immunocompromised individuals. Approximately 5% of patients with nontyphoid *Salmonella*-related gastrointestinal illness, whether overt or subclinical, are expected to develop potentially fatal bacteremia [1]. Virtually any anatomical site may be invaded by nontyphoid *Salmonella* via hematogenous spread and evolve into local infection. Although most *Salmonella* infections are self-limiting, *Salmonella enterica* serotype *choleraesuis* (*S. choleraesuis*) is extremely invasive and carries a predisposition to cause bacteremia and metastatic local infections in humans. Thus, prompt parenteral antimicrobial therapy is required [2].

Autosomal dominant polycystic kidney disease (ADPKD) is the most common of the inherited renal cystic diseases, and infection is one of the most common causes of death in these patients. Cyst infections in ADPKD patients on hemodialysis (HD) are not unusual but are often difficult to diagnose and treat. Most cyst infections result from retrograde passage of bacteria from the bladder to kidney but can occur by hematogenous seeding as well

Fig. 1. One predominant cyst (9 cm) is noted in the lower pole of the left kidney with high-density content and thickened wall (*). Some perirenal strands bulging out are noted (white arrow). This cyst is drained by an indwelling catheter.

[3]. Gram-negative bacteria comprise most of the causative organisms [4]. Still, renal cyst infection secondary to *Salmonella* species in ADPKD patients has rarely been described.

Morbidity and mortality are substantially increased in dialysis patients developing *Salmonella* enteritis and septicemia [5]. Eradicating *Salmonella* renal cyst infection in ADPKD patients on HD may be difficult in terms of extensively metastatic spread, poor antibiotic penetration into the cysts and immunocompromise caused by uremia. This is the first report describing intracystic antibiotic infusion as a potential salvage therapy in treating refractory renal cyst infection caused by *S. choleraesuis*, a highly virulent pathogen, in an ADPKD patient on HD.

Case Report

A 52-year-old male presented at the Emergency Care Unit with complaints of shortness of breath and chest tightness during the previous 2 days. The patient had a history of hypertension and had been undergoing HD for uremia caused by ADPKD for 2 years.

He recalled experiencing one episode of acute gastroenteritis with a 3-day course of fever, intermittent abdominal cramping pain and diarrhea 7 days earlier which remitted without antibiotic treatment. The patient was hospitalized for acute pulmonary edema and cardiac arrhythmia related to hyperkalemia, and his symptoms abated rapidly after emergency HD. Analyses of urine and stool specimens investigated on admission were unremarkable.

On day 3 of hospitalization, the patient had fever with chills but there was no associated abdominal pain, dysuria or diarrhea. A complete blood count revealed leukocytosis with a white blood cell (WBC) count of $15,200/\mu\text{l}$ and 86% neutrophils. Empirical antibiotic with intravenous ceftriaxone (1 g/12 h) was prescribed. Despite the ceftriaxone therapy, the patient remained febrile and suffered general discomfort. On day 7, WBC count and C-reactive protein were $17,400/\mu\text{l}$ and 91.9 mg/l, respectively. The urine culture obtained on day 1 showed no growth; however, blood and stool cultures both yielded *S. choleraesuis*, which was susceptible to ciprofloxacin (CIP) and imipenem but resistant to ampicillin, ceftriaxone, chloramphenicol and trimethoprim-sulfamethoxazole. To investigate a probable metastatic infection, renal ultrasonography was performed and showed echogenic debris and/or a fluid-fluid level within multiple cysts in the left kidney indicating infected cysts. Abdominal computerized tomography (CT) disclosed multiple cysts in the left kidney that were highly dense with thickened walls measuring up to 9 cm in the lower pole (fig. 1). During percutaneous CT-guided catheter drainage of the largest cyst, yellowish-brown purulent fluid was obtained. Laboratory investigation of the fluid showed a WBC count of $2.26 \times 10^5/\mu\text{l}$ and a red blood cell count of $1.56 \times 10^4/\mu\text{l}$, which confirmed a pyocyst. Intravenous CIP (200 mg/12 h) therapy was then prescribed in place of ceftriaxone, and the fever subsided thereafter.

On day 12, the cyst fluid cultures yielded *S. choleraesuis*, which was susceptible to CIP. Although the patient had become afebrile, the repeated microscopic analyses of the drained fluid showed a purulent appearance, and repeated renal echography showed residual echogenic debris and thick septae within these infected cysts. On day 17, he developed recurrent fever with an increase in leukocytosis (WBC, $18,700/\mu\text{l}$) and a very high C-reactive protein of 113 mg/l. In order to achieve complete eradication for this refractory patient, intracystic infusion of diluted CIP (5 mg/dl, with the infusion volume of 50% of the drained fluid volume on day 7 and indwelling time of 12 h) via the drainage tube was administered twice a day for 7 consecutive days. By this measure, the subsequent fluid drained from the polycystic kidney became clearer gradually, and microbiological culture did not yield any growth. The drainage catheter was removed after a 21-day course of intravenous CIP which was switched to oral CIP (250 mg/12 h) thereafter. The patient was discharged after completing the 4-week course of CIP. Follow-up abdominal CT and renal ultrasonography did not show any residual pyocyst. The patient did not experience recurrence during the 6-month follow-up period.

Discussion

Endovascular infection and deep bone or visceral abscesses are important complications relating to *Salmonella* gastroenteritis and may be life-threatening [1]. Our

patient was an immunocompromised patient with underlying ADPKD undergoing HD for uremia. The *Salmonella* infection in this patient was severe and resulted in bacteremia and formation of multiple pyocysts; however, febrile reaction with general discomfort was the only manifestation. For this patient, a systemic workup for the potential sites of metastatic infection is of critical importance and renal cyst infection should be considered in ADPKD patients undergoing HD with *Salmonella* bacteremia even without the presence of overt symptoms. In addition to intravenous antibiotic therapy, aspiration or catheter drainage of local purulent materials is usually indicated.

When treating severely ill patients or those with risk factors for extraintestinal spread related to *Salmonella* infection, antimicrobial therapy should be initiated after obtaining appropriate blood and fecal cultures. Usually, 3–7 days of treatment are sufficient [1]. Additionally, prompt antimicrobial therapy is also essential in the treatment of *S. choleraesuis* infection because of the high rate of extraintestinal infections caused by this organism [2]. Lipophilic antibiotics such as trimethoprim-sulfamethoxazole and the fluoroquinolones are effective agents for penetrating the cyst when treating renal cyst infection [6, 7], and also good choices for *Salmonella* infection [1]. However, the effect of intravenous CIP to penetrate renal cysts in this ADPKD patient on HD remained uncertain, and treatment failure may result from insufficient intracystic antibiotic concentration. In Taiwan, there has been a steady increase in the number of reported cases of *S. choleraesuis* sepsis, and the emergence of

antimicrobial-resistant strains further complicates the treatment of renal cyst infection of our patient [8]. Another important issue is that invasive surgical interventions (e.g. nephrectomy) should be considered in refractory patients to prevent serious complications or even death [9]. However, our case report suggests intracystic antibiotic infusion in patients with refractory renal cyst infection is a potential salvage treatment and unilateral nephrectomy can be prevented. Although the optimal concentration of CIP for intracystic infusion needs further investigation, the concentration of 5 mg/dl in this patient is the same as the intraperitoneal CIP dosing recommendations for peritonitis in continuous ambulatory peritoneal dialysis patients [10].

The complete eradication of *S. choleraesuis* in our patient may be attributed to the achievement of sufficient target tissue levels by intracystic CIP infusion. Intracystic infusion of antibiotic appears to be advantageous in the treatment of refractory renal cyst infection related to a highly virulent pathogen (e.g. *S. choleraesuis*) or extensive involvement in patients with ADPKD.

Conclusion

In this patient, intracystic infusion of CIP achieved sufficient antibiotic levels in infected renal cysts and hence completely eradicated *S. choleraesuis*. Therefore, intracystic antibiotic infusion could be a potential salvage therapy for refractory renal cyst infection.

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