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**Title: Abscess caused by *Citrobacter koseri* infection: Three case reports and a literature review**

**Running title: *Citrobacter koseri* abscess**

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## **Abstract**

In this report, we present 3 cases of abscess caused by *Citrobacter koseri*. All infected patients recovered after initial empirical antibiotic treatment and percutaneous drainage of the abscess. We reviewed the literature and found 9 adult cases of *C. koseri* abscess. In most of these cases, patients recovered after timely antibiotic treatment and drainage.

**Keywords:** *Citrobacter koseri*, sepsis, renal abscess, iliopsoas abscess

## Introduction

*Citrobacter* species, belonging to the family Enterobacteriaceae, are environmental organisms commonly found in soil, water, and the intestinal tracts of animals and humans. *Citrobacter* infections usually occur in hospital settings in patients with multiple co-morbidities and seldom cause disease in the general population (1). Neonates and immunocompromised hosts are highly susceptible to *Citrobacter* infections, which are mainly caused by *Citrobacter freundii* and *Citrobacter koseri*. *C. freundii* is usually associated with hepatobiliary tract infections, while *C. koseri* causes neonatal meningitis and brain abscess with high mortality rates (2). Few cases of *C. koseri* causing severe infections or abscess in adults have been reported. In this report, we present 3 cases of *Citrobacter* abscess at different sites in adults. Unsatisfactory outcomes were obtained with initial conservative treatment, but complete recovery was achieved after invasive intervention combined with medication.

### Case 1

A 72-year-old man with hepatitis B virus-related cirrhosis presented with fever and right thigh swelling for 5 days. On arrival, his body temperature was 37°C, blood pressure was 111/68 mm Hg, pulse was 108 beats per minute, and respiration rate was 20 breaths per minute. Physical examination revealed local heat and tenderness over the right thigh area. Laboratory studies showed C-reactive protein concentration of 15.6 mg/dL (normal level, <0.8 mg/dL). Other laboratory results were unremarkable. Computed tomography (CT) revealed diffuse subcutaneous edema of the right thigh. The initial choice of empirical antibiotic was intravenous (i.v.) cefmetazole administered at a dose of 1 g every 8 h. Blood and urine cultures yielded mucoid

colonies on sheep blood agar after 24 h of incubation in 5% CO<sub>2</sub> at 35°C. The biochemical profile identified the organism as *C. koseri*. The minimal inhibitory concentrations determined by antibiotic susceptibility tests were as follows: gentamicin, <2 µg/ml (susceptible); cefazolin, <4 µg/ml (susceptible); ciprofloxacin, <0.5 µg/ml (susceptible); and imipenem, <1 µg/ml (susceptible). Despite treatment with i.v. ciprofloxacin at a dose of 400 mg every 12 h, prescribed based on culture results, the patient had continuous undulating fever and progressive low abdominal pain. CT disclosed a low-density mass in the right psoas muscle (Fig. 1). CT-guided percutaneous drainage was performed for this abscess of the psoas muscle. Culture from the abscess confirmed growth of *C. koseri*. Colonoscopic examination was normal. Treatment with i.v. ciprofloxacin (400 mg every 12 h for 4 weeks) was administered, and the drainage tube was removed after complete resolution.

## Case 2

A 40-year-old, previously healthy woman, was transferred to our hospital with a 10-day history of fever with chills. She had taken amoxicillin/clavulanic acid (1 g twice daily for 7 days), but the fever persisted. On arrival, she had a blood pressure of 103/74 mm Hg, pulse rate of 76 beats per minute, body temperature of 38.4°C, and respiratory rate of 18 breaths per minute. On physical examination, tenderness over the right lower quadrant of the abdomen was noted. Initial laboratory tests were all normal except for high C-reactive protein level of 7.4 mg/dL (normal level, <0.8 mg/dL) and high erythrocyte sedimentary rate (ESR) of 85 mm/h. Blood culture revealed no growth. CT of the abdomen showed one 1.5 × 2.1-cm abnormal fluid accumulation in the right iliopsoas muscle with rim enhancement (Fig. 2). The patient received ultrasound-guided drainage and cefmetazole at a dose of 1 g every 6 h.

Culture of the aspirated pus revealed *C. koseri*. The susceptibility test results were the same as reported in case 1. Additionally, *C. koseri* displayed resistance to ampicillin but sensitivity to amoxicillin/clavulanic acid. No abnormal lesion was noted on colonoscopy. After completing a 14-day course of i.v. cefmetazole (1 g every 6 h) and drain removal, the patient was discharged with oral ceftibuten (200 mg twice daily for 14 days). She had no more fever or abdominal pain, and the ESR decreased gradually from 85 to 27 mm/h.

### Case 3

A 51-year-old diabetic woman presented with a 1-day complaint of fever and right flank pain. Her medical history included right nephrolithiasis and 3-vessel coronary artery disease. Her body temperature was 38.6°C, blood pressure was 96/61 mm Hg, pulse rate was 106 beats per minute, and respiration rate was 26 breaths per minute with a deep pattern. Laboratory studies showed a leukocyte count of  $2.6 \times 10^4/\mu\text{L}$  (normal range,  $3$  to  $9 \times 10^3/\mu\text{L}$ ), C-reactive protein level of 20.7 mg/dL (normal level, <0.8 mg/dL), blood urea nitrogen level of 50 mg/dL (normal range, 5 to 26 mg/dL), serum creatinine level of 4.18 mg/dL (normal range, 0.5 to 1.3 mg/dL), glucose level of 600 mg/dL, lactate level of 48.0 mg/dL (normal range, 4.5 to 19.6 mg/dL), and ketone level of 0 mg/dL. Arterial blood gas analysis showed metabolic acidosis with pH 7.44, bicarbonate level of 14.2 mmol/dL (normal level, 24 mmol/dL), and anion gap of 36 mmol/dL (normal range, 10 to 12 mmol/dL). Urinalysis revealed numerous leukocytes. Abdominal ultrasound showed one  $1.7 \times 2$ -cm hypoechoic lesion over the right kidney without liver involvement. CT of the abdomen revealed a focal area of low density in the right renal parenchyma, with swelling in the involved portion and perirenal fat stripping. As treatment, i.v. flomoxef (1 g once daily) was administrated

empirically. The blood culture yielded *C. koseri*, and the sensitivity test results were the same as those in case 1. Based on the test results, we changed the antibiotic to i.v. cefazolin (500 mg every 12 h for 14 days). The patient was discharged thereafter, with oral cefradine (500 mg twice daily). However, she discontinued the use of oral cefradine and refused further outpatient follow-up. Septic shock developed weeks later. Non-enhanced CT showed a gas-forming abscess in segment 5–6 of the liver and a right renal abscess of 4.7 × 7.3 cm (Fig. 3A and 3B). CT-guided percutaneous drainage was performed for the abscesses of the kidney and liver. Cultures of urine, blood, and the aspirated pus showed *C. koseri* growth, and antimicrobial susceptibility test results matched those from the patient’s previous admission. Anaerobic culture of the pus revealed no growth. She was treated with i.v. ciprofloxacin (400 mg once daily for 4 weeks), and the drainage tube was removed after complete resolution. Oral ciprofloxacin (500 mg every 12 h) was prescribed for another month until the ESR decreased from >140 mm/h to a steady state of 60 mm/h. After 4 months of follow-up, the patient was asymptomatic and without detectable abscesses.

## **Discussion**

*C. koseri* (previously classified as *Citrobacter diversus*) has long been recognized to be a cause of abscess in neonates. The literature about *Citrobacter* abscess in adults, however, is scanty (3). We performed a PubMed search with the terms “*Citrobacter koseri*,” “*Citrobacter diversus*,” and “abscess.” Nine cases of abscess secondary to *C. koseri* infection in adults were found in this search (Table 1) (4-12).

Cases 1 and 2 are the first reports describing favorable therapeutic outcomes for iliopsoas abscess caused by *C. koseri*. Iliopsoas abscess commonly occurs because of hematogenous spread from an occult source. *Staphylococcus aureus* is the leading

causative organism. Iliopsoas abscess can also result from diseases of the genitourinary, gastrointestinal, or musculoskeletal systems, of which *Streptococcus* species and *Escherichia coli* are the 2 main causative pathogens (13). Iliopsoas abscess caused by *C. koseri* is, however, unusual. Vichib et al. described a retroperitoneal abscess caused by *C. koseri* that was lethal despite surgical drainage. Mortality in that case was attributed to an acute pulmonary event during sepsis (5). In treating iliopsoas abscesses less than 3 cm in diameter in immunocompetent patients, prolonged treatment (for weeks) with antibiotic alone can offer successful recovery (14). According to Witzigmann et al., Bufalari et al., and McClean et al., patients with iliopsoas abscess might benefit from directed drainage (15-17). Among our cases, both patients with iliopsoas abscess showed remarkable recovery after percutaneous drainage and prompt antibiotic treatment.

With regard to case 3, urolithiasis and diabetes mellitus are 2 predisposing factors of renal abscess (18). A renal abscess usually results from an ascending infection. Renal abscess due to *Citrobacter* species is rare. Williams and Simmons described a case of *Citrobacter* perinephric abscess in a transplant recipient in 1974 (4). Our case is the first report of concurrent renal and liver abscesses caused by community-acquired *C. koseri* in a diabetic patient. Although initially the renal abscess was small (less than 2 cm in diameter) and responded well to i.v. antibiotics during the first admission, the patient subsequently developed overwhelming septicemia, a liver abscess, and an enlarged renal abscess. The tendency of *C. koseri* to form brain abscesses in neonates is recognized and is attributed to a specific 32-kD outer membrane protein of *C. koseri* and the immature neonatal brain blood barrier (3). Until now, though, there has been no known predisposition of *C. koseri* to form abscesses in adults. Thus, we suspect that the deteriorating infection in case 3 is

related to the discontinuation of antibiotics and, most importantly, the lack of drainage during the first admission.

Instillation of antibiotic into abscesses does not improve the outcome in cases of *Citrobacter* infections. Different species of *Citrobacter* show different antimicrobial susceptibility profiles. These profiles should be referenced when choosing antibiotics to treat serious diseases. *C. koseri* is typically resistant to ampicillin but susceptible to aminoglycosides. In case 2, the initial undulating fever might have been due to a lack of direct drainage rather than  $\beta$ -lactam resistance. In *C. koseri* infection, aminoglycosides, carbapenems, fluoroquinolones, and third- or fourth-generation cephalosporins are considered effective, but some *C. koseri* strains may develop isolated resistance to  $\beta$ -lactams, aminoglycosides, and aztreonam (19). Thus, Shih et al. have proposed that a combination of  $\beta$ -lactams and aminoglycosides would be better at treating *Citrobacter* bacteremia than would a single agent (20). Until now, there has been no agreement on the use of monotherapy or combinations of antibiotics in treating *Citrobacter* abscesses. Empirical combination therapy would be appropriate in cases of shock, neutropenia, or nosocomial *Citrobacter* infections (21, 22).

Doran stated that it would be proper to initiate treatment of neonatal brain abscess with direct aspiration or drainage followed by antibiotics for 4 to 6 weeks (23).

Among the 12 patients listed in Table 1, all 10 cases of contracted community-acquired *Citrobacter* infections received direct drainage or surgical intervention and cephalosporins, aminoglycosides, fluoroquinolones, or  $\beta$ -lactams, alone or in combination. At the end of therapy, 11 cases resolved completely, and 1 resulted in death.

*Citrobacter* species is not only a nosocomial pathogen but also a causative agent



of community-acquired infection. We have presented 3 cases to prompt a clinical alert to the possibility of *C. koseri* abscess, even in immunocompetent people.

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