Liver abscess with *Citrobacter koseri* bacteremia

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SUMMARY

Citrobacter koseri is a rare cause of liver abscess with two reported cases in diabetic patients. We report a rare case of *C. koseri* liver abscess with *C. koseri* bacteremia in an elderly male with chronic kidney disease. He presented vomiting and weakness without any other signs. He was diagnosed with liver abscess by ultrasound, and blood culture showed *C. koseri* growth. The patient was treated effectively with a course of antibiotics and drainage. When *C. koseri* is isolated in patients with comorbidity, such as chronic kidney disease, we should consider the possibility of abscess including liver abscess and utilize a combined treatment of drainage and course of antibiotics for mixed infection.

Keywords: *Citrobacter koseri*, liver abscess, drainage

INTRODUCTION

Citrobacter koseri (*C. koseri*) is an environmental Gram-negative bacterium which colonizes the human gastrointestinal tract [1]. It is recognized to be a cause of abscess in neonates, and in adult patients, infections usually occur with underlying comorbidities or immunosuppression [2, 3]. Although the potential virulence of the species is considered low, it can cause serious nosocomial infection.

A small number of cases of abscess in adults have been reported [3]. Of these, to the best of our knowledge, there are only two case reports of liver abscess caused by *C. koseri* [3, 4]. Both cases were liver abscesses occurring in patients with diabetes mellitus. The first case, a serious infection, occurred following incomplete treatment for right renal abscess [3]. The second case, an anatomical abnormality in the biliary system, had a previous operation for periampullary carcinoma [4].

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Here, we report a case of an 82-year-old male with chronic kidney disease, intraductal papillary mucinous neoplasm (IPMN) and chronic pancreatitis, who presented vomiting and weakness and who was diagnosed with liver abscess concurrent with *C. koseri* detected in the blood.

CASE REPORT

An 82-year-old male patient came to the emergency room following two days of vomiting and weakness. On arrival, he was alert and conscious. Body temperature was 38.9°C, blood pressure 102/83 mmHg, pulse rate 106/min, respiratory rate 20/min and oxygen saturation 95% on ambient air. His height was 162 cm, weight 59.8 kg. Systemic examination was unremarkable, except for right-side costo-vertebral angle knock pain. The patient had a medical history of chronic kidney disease, IPMN and chronic pancreatitis, but not of diabetes mellitus. He had abdominal aortic aneurysm replacement surgery six years previously. He also had a pack-year history of tobacco use until quitting 20 years before and he no longer drank alcohol, having stopped 10 years previously.

Blood tests on admission day revealed leukocytosis with leukocyte count of 15,120 /mm^3, anemia with hemoglobin at 9.2 g/dL and platelet count at 149,000/mm^3. Liver functions were normal, alanine transaminase at 14 U/L, aspartate transaminase at 25 U/L, alkaline phosphatase at 308 U/L and gamma glutamyl transpeptidase at 83 U/L with normal bilirubin and albumin levels. The patient had normal coagulation profile (prothrombin time: 13.9 s). Random blood glucose was 136 mg/dL. Kidney function test revealed blood urea nitrogen at 31.6 mg/dL and serum creatinine at 2.49 mg/dL. Serum sodium level was 139 mEq/L and potassium level was 4.4 mEq/L. The patient had C-reactive protein (CRP) of 4.7 mg/dL and serum lactate level of 1.7 mmol/L. Urinalysis was negative for leukocytes and nitrate. Non-contrast CT showed cystic region consistent with previously diagnosed IPMN in the pancreatic neck. It also revealed chronic pancreatitis with pancreatic stones and liver cyst in the left lobe. Contrast-enhanced CT was avoided because of the patient's creatinine level. Transthoracic echocardiogram showed no vegetation. On day three, blood culture showed growth of Gram-negative rods, which revealed *C. koseri*. On the same day, abdominal ultrasonography showed a heterogeneous lesion in the liver measuring 27×25 mm with liquefaction in the right lobe (Figure 1), which was unclear on CT on day one.

We observed the patient without antibiotic therapy because of a quick sequential organ failure assessment score of zero and no elevation of lactate (5). On days one and two, the patient's condition was stable. On day three, the patient was started on intravenous cefmetazole at 1g every 12 hours which was adjusted to the renal insufficiency [the creatinine level 2.67 mg/dL, creatinine clearance (CCr) estimated by Cockcroft-Gault equation 16.8 mL/min], after blood culture showed growth of Gram-negative rods. On day six, *C. koseri* was identified with oxidase-negative fermentation of glucose by triple sugar iron agar (Nissui), indole-positive by SIM Medium (Nissui), citrate utilization by Simmons' citrate agar (Eiken), Voges-Proskauer test negative by VP agar (Eiken), ornithine decarboxylase positive and lysine decarboxylase negative by Ornithine-Indol-Mobility-Lysine agar (Eiken). It was also identified by ID Test EB-20 (Nissui). The antibiotics were therefore changed to intravenous ciprofloxacin at 300 mg every 24 hours adjusted to the renal insufficiency (creatinine level 2.67 mg/dL, CCr 16.8 mL/min), with reference to the susceptibility results (Table 1), which were tested by dry plate (Eiken) for enterobacteriaceae. On day seven, percutaneous needle aspiration was

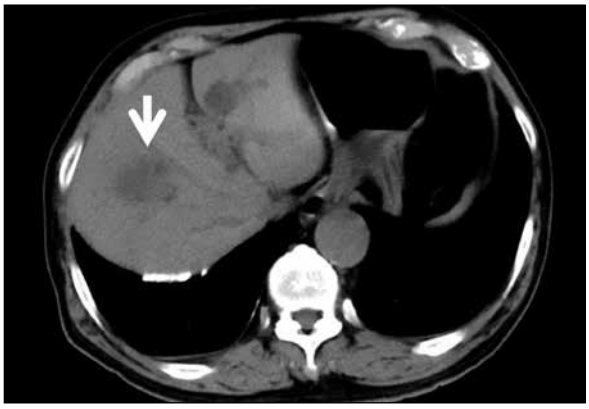

Figure 1 - Abdominal ultrasonography shows a heterogeneous lesion in the liver measuring 27×25 mm with liquefaction in the right lobe (arrow).

Table 1 - Susceptibility of *Citrobacter koseri* isolated in our patient.

Antibiotics	*Minimum inhibitory concentration (mg/mL)*	*Susceptibility*
Cefazolin	<1	Susceptible
Cefotiam	<1	Susceptible
Ceftriaxone	<1	Susceptible
Ceftazidime	<1	Susceptible
Cefepime	<1	Susceptible
Cefcapene	<0.5	Susceptible
Cefmetazole	<2	Susceptible
Flomoxef	<1	Susceptible
Imipenem	<0.25	Susceptible
Panipenem	<0.25	Susceptible
Ampicillin	>16	Resistant
Piperacillin	32	Intermediate
Sulbactam/ Ampicillin	2	Susceptible
Amikacin	<1	Susceptible
Minocycline	<1	Susceptible
Fosfomycin	<32	Susceptible
Levofloxacin	<0.12	Susceptible
Ciprofloxacin	<0.25	Susceptible

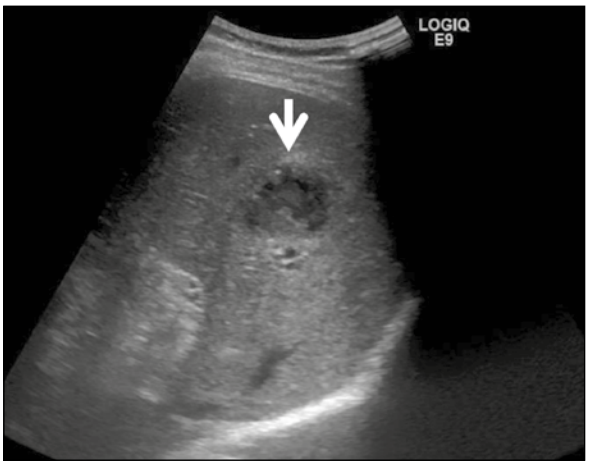

Figure 2 - CT of the abdomen shows enlargement of liver abscess measuring 33 mm in the right lobe (arrow).

performed unsuccessfully. Intravenous ciprofloxacin was continued and the patient remained afebrile. The treatment was therefore thought to be effective. On day 15, however, the patient appeared to have fever and rigor. CT showed enlargement of the liver abscess measuring 33 mm at its widest point (Figure 2). The possibility of resistance of *C. koseri* to ciprofloxacin caused by another organism was considered, including mixed infection or inadequate control of the source of infection. Meropenem at 0.5 g every 12 hours adjusted to the renal insufficiency (creatinine level 2.44 mg/dL, CCr 18.4 mL/min) was started and the liver abscess was drained under ultrasound guidance for two days. Treatment was effective; the patient improved and remained afebrile. Culture of aspirate was negative, so meropenem was discontinued, while intravenous ciprofloxacin was continued on day 18. The patient remained afebrile and the abscess became smaller. On day 28, the patient was discharged and prescribed oral ciprofloxacin for another four weeks.

DISCUSSION

This case of *C. koseri* infection introduces two important clinical issues. Liver abscess associated with *C. koseri* can easily become serious. Moreover, liver abscess requires both antibiotic therapy and drainage, even if the size of abscess is too small to perform aspiration or drainage at first.

C. koseri is a member of the genus Citrobacter which causes human diseases [3]. It has caused frequent nosocomial outbreaks of neonatal meningitis. In several instances, outbreaks have been accompanied by high rates of intestinal colonization by the organism in infants and by bacterial transmission via the hands of health care workers [6]. In adults, however, 10 of reported 12 cases of *C. koseri* abscess were community-acquired [3]. Furthermore, *C. koseri* liver abscess is rare. To our knowledge, the present case is only the third reported case of liver abscess associated with *C. koseri*.

Lin et al. reported a case of a 51-year-old female with known history of diabetes mellitus suffering from renal abscess caused by *C. koseri*-accompanied liver abscess afterwards [3]. She first had right renal abscess without hepatic involvement and with detected *C. koseri* bacteremia. She was treated with a course of antibiotics. The patient was discharged with oral antibiotics, but she discontinued them and refused further outpatient follow-up. Septic shock developed weeks later with right renal abscess and liver abscess. She was treated with antibiotics and CT-guided percutaneous drainage for the abscesses of both the kidney and the liver.

Gupta, et al. reported a case of a 56-year-old male with diabetes mellitus who underwent operation for periampullary carcinoma 20 years previously [4]. He had been febrile for one week, and was managed with parenteral antibiotics, repeated aspiration of liver abscess, and drainage.

The present case was liver abscess with community-acquired *C. koseri* bacteremia, which was the same strain as the reported two cases. The patient did not have diabetes mellitus, but had medical history of chronic kidney disease, IPMN, and chronic pancreatitis. He had *C. koseri* bacteremia and liver abscess. We suspected that the abscess was associated with *C. koseri* despite liver abscess culture was negative because the patient was already under antibiotics treatment at the moment of the microbiological examination. All three cases required drainage, despite patients being started on adequate antibiotics treatment.

The first case of liver abscess, reported by Lin et al., resulted in serious infection due to interruption of antibiotics intake, which may have led to the dissemination of *C. koseri* to other body parts. On the other hand, the second case, reported by

Gupta et al., had an operation for periampullary carcinoma.
The present case, meanwhile, had IPMN and chronic pancreatitis.
We suspect, therefore, that anatomical abnormality could be the underlying condition in *C. koseri* liver abscess cases. All three reported cases eventually needed aspiration or drainage, despite adequate antibiotic therapy as per sensitivity report. Given the rarity of this disease, however, further investigations are required.
Resistance to broad-spectrum antibiotics is one treatment dilemma for *Citrobacter* infections. *C. freundii* strains, like strains of *Enterobacter* and *Serratia*, have inducible ampC genes encoding resistance to ampicillin and first-generation cephalosporin that can be produced constitutively at high levels after mutations [7]. In one report, a diabetic patient had necrotizing fasciitis caused by *C. freundii*, which became resistant to cefotaxime within five days [7]. In addition, like members of these other genera, isolates of *Citrobacter* may be resistant to other antibiotics as a result of plasmid-encoded resistance genes [6]. There are reports of *C. koseri* isolates bearing extended-spectrum beta-lactamase (ESBL) genes and carbapenemase [1, 8-10]. The present case was successfully treated without the bacterium becoming resistant to antibiotics.
This is a rare case that highlights liver abscess with *C. koseri* bacteremia in a patient with chronic kidney disease, IPMN and chronic pancreatitis requiring drainage for successful treatment. He was started on a seemingly adequate, but ineffective course of antibiotic therapy. When *C. koseri* is isolated in patients with comorbidity like chronic kidney disease, we should consider the possibility of abscess, including liver abscess.
Liver abscess-associated *C. koseri* is rare. When it occurs, a combination treatment of drainage and course of antibiotics should be considered. Combined treatment should be targeted to include anaerobes, even when the abscess is small and no other organisms are isolated. Further reports are needed to clarify the clinical features of *C. koseri* liver abscess.

Conflicts of interest
None

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