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# Infective Endocarditis Due to *Citrobacter koseri* in an Immunocompetent Adult▽

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***Citrobacter koseri*** **(formerly *Citrobacter diversus*) is a motile gram-negative bacillus usually arising from urinary and gastrointestinal tracts. *C. koseri* rarely causes infection in immunocompetent patients and, thus far, has been considered an opportunistic pathogen. We report on a 30-year-old man, with no medical past, hospitalized for infective aortic endocarditis due to *C. koseri*. Four weeks of antibiotherapy led to a full recovery for this patient. However, this case is unusual, as previous history and 1 year of follow-up showed no features of intercurrent immunosuppression. Microbiological diagnosis was based on using 16S rRNA gene sequencing.**

## CASE REPORT

A 30-year-old man, previously healthy, was admitted to the hospital after 3 weeks of fever, night sweats, and a 2-kg weight loss. He was admitted to the hospital due to intense diffuse myalgia, left ankle arthritis, and abdominal pain. He did not have a history of cardiac or general disease and reported no intravenous drug abuse.

The clinical examination on admission showed a temperature of 39.7°C and splenomegaly combined with hepatomegaly. Cardiac auscultation found an unknown aortic regurgitation murmur. There were no signs of severe sepsis or congestive heart failure.

Laboratory examinations showed a leukocyte count of 20.485 cells/mm$^3$ and a significantly elevated C-reactive protein level of 109 mg/liter. Blood samples were inoculated in aerobic and anaerobic blood culture vials (BacT/Alert 3D; bioMérieux, Marcy l'Etoile, France). Three aerobic and anaerobic vials, obtained prior to antibiotic administration, were positive and were subcultured onto nutrient agar at 37°C. The agar plates were incubated for 24 h, and colonies of gram-negative bacilli were isolated. Isolates were identified as *Citrobacter koseri* using API 20E strips (bioMérieux, Marcy l'Etoile, France), as recommended by the manufacturer. *Citrobacter koseri*/*Citrobacter amalonaticus* (code no. 3344513; percentage of identification = 99.9%; index of typicity = 1.0) were the bacteria repeatedly identified with the API 20E strips. To confirm the identification, the 16S rRNA gene sequence of the isolate was determined as previously described (3, 4). Briefly, the 16S rRNA gene was amplified by PCR with primers Ad (5′-AGAGTTTGATC[A/C]TGGCTCAG-3′) and rJ (5′-GGTTACCTTGTTACGACTT-3′). We determined 1,000 continuous nucleotides of the 16S rRNA gene sequence. We compared the complete 16S rRNA gene sequence of the isolate with all of the bacterial sequences available from the GenBank database using the BLAST program (National Center for Biotechnology Information): our sequence showed 99% similarity to that of the *Citrobacter koseri* ATCC BAA-895 type strain (GenBank accession no. CP000822). The antimicrobial susceptibility of the isolate was studied by the disk diffusion method on Mueller-Hinton agar, according to the guidelines of the AST Committee of the French Society for Microbiology (http://www.sfm.asso.fr). Disks were purchased from Bio-Rad (Marnes-la-Coquette, France). The following 25 antimicrobial agents were tested: amoxicillin (amoxicilline), amoxicillin-clavulanate, ticarcillin, ticarcillin-clavulanate, piperacillin, piperacillin-tazobactam, cefalotin, cefoxitin, cefotaxime, ceftazidime, cefepime, aztreonam, imipenem, gentamicin, tobramycin, netilmicin, amikacin, tetracycline, chloramphenicol, co-trimoxazole, nalidixic acid, pefloxacin, ciprofloxacin, rifampin (rifampicin), and fosfomycin. The isolate was resistant to amoxicillin, ticarcillin, and rifampin. The isolate had intermediate resistance to piperacillin and was susceptible to all other antibiotics tested. The MICs for four antibiotics were also determined by the agar diffusion method using the Epsilometer test (Etest; AB Biodisk, Solna, Sweden) on Mueller-Hinton agar, as recommended by the manufacturer. The MIC results were as follows: cefotaxime, 0.064 mg/liter; ceftriaxone, 0.064 mg/liter; gentamicin, 0.38 mg/liter; and rifampin, 24 mg/liter.

Transesophageal echocardiography revealed an aortic regurgitation without evidence of mature vegetation on the aortic valve. Computed tomography of the heart did not show an aortic annulus abscess. Abdominal computed tomography identified a spleen abscess. Thus, the patient was diagnosed with aortic endocarditis due to *C. koseri*, according to the endocarditis diagnostic criteria of Durack et al. (2).

Urine examination, stool culture, and colonoscopy were unable to determine the primary source of infection. Magnetic resonance imaging of the left ankle found no features of osteoarthritis. No immunosuppressive factors, such as diabetes, human immunodeficiency virus, lymphopenia, hypogamma-

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globulinemia, or hypocomplementemia, were reported. Also, the patient was not an intravenous drug user.

Patient treatment included intravenous ceftriaxone (1 g twice a day) for 4 weeks combined with 5 days of amikacin. Clinical recovery (fever disappeared in 2 days, and the heart murmur disappeared within 2 weeks), negative blood cultures, and the disappearance of aortic regurgitation were reported. The patient did not have a relapse of infection or a recurrence of the regurgitation murmur during the first year of follow-up.

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**Discussion.** Members of the *Citrobacter* genus are motile, facultative, and anaerobic gram-negative bacilli that belong to the *Enterobacteriaceae* family. There are three species in the genus *Citrobacter* which are known to be pathogenic in humans, as follows: *C. amalonaticus*, *C. diversus*, and *C. freundii*. Recently, *C. diversus* has been renamed *Citrobacter koseri*. The genus is distributed in soil, water, and food, as well as in human and animal intestinal tracts. These species cause various infections in humans involving the urinary, gastrointestinal, and respiratory tracts. Infections are commonly reported in neonates, the elderly, and immunocompromised or debilitated hosts. A few cases of infective endocarditis, mostly on the right side, have previously been reported. We report a case of aortic endocarditis in an immunocompetent patient without underlying valvular disease. In humans, *Citrobacter* spp. are implicated mainly in urinary tract infections (46%), respiratory tract infections (16%), blood cultures (16%), and pus (12%) (7). *C. koseri* is also associated with retroperitoneal abscess, pneumonia, gastroenteritis, meningitis, and bacteremia in humans (1, 5, 9). In adults, infections are reported mainly in immunocompromised patients, but 11% of patients exhibit no underlying disease (7, 1).

*C. koseri* rarely causes endocarditis. To our knowledge, there are three previous cases in the literature (6, 10, 11). The following two of the three cases presented favorable conditions: one patient had a pacemaker and the other was an intravenous drug user. Our patient did not match these conditions at admission or during the 1-year follow-up. With our patient, we did not find the germ in feces at the time of infection. *C. koseri* is a commensal bacterium of the digestive tract, which can be isolated from the stool, without pathological manifestations. Treatment of patients with antibiotherapy may be difficult in these types of cases, as some strains have acquired a mechanism of resistance like TEM- and SHV-type extended-spectrum β-lactamases (8).

**Conclusion.** *C. koseri* endocarditis is rare in adults, particularly in nonimmunocompromised patients. This is the first report confirming infection by *C. koseri* using 16S rRNA gene sequencing.

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