

# *Citrobacter koseri* Infective Endocarditis in an Immunocompetent Male Successfully Treated with Valve Replacement and a Shortened-Course of Antimicrobial Therapy: A Case Report

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## Abstract

**Background:** *Citrobacter koseri* is a rare cause of infective endocarditis (IE), especially in immunocompetent individuals. We present a case of acute IE of the native mitral valve caused by *C. koseri* in a 61-year-old Filipino man successfully treated with valve replacement and shortened-course of antimicrobial therapy. **Case Presentation:** The patient presented with fever, delirium, cardiac symptoms, leukocytosis and elevated procalcitonin. He was given meropenem and vancomycin as empiric therapy, Blood cultures identified *C. koseri*. A transesophageal echocardiogram confirmed the presence of a large, mobile vegetation measuring 1.399 cm attached to the anterior mitral valve leaflet. Given the patient's multiple risk factors for embolization, including a vegetation size greater than 10 mm, vegetation mobility, vegetation location on the anterior mitral valve leaflet, and the possibility of prior embolization, the patient underwent a successful valve replacement. Vegetation attached to the anterior mitral valve leaflet was visualized intraoperatively. There was no paravalvular extension of infection, annular abscess, or destructive penetrating lesion (fistula). Postoperatively, fever lysed, and inflammatory markers improved. Postoperative blood cultures were sterile. Cultures of the excised anterior mitral valve leaflet were negative for bacterial growth, likely due to the targeted antimicrobial therapy administered before surgery. Following a series of therapies, the patient was discharged with a three-week course of continuous intravenous meropenem therapy to complete the treatment regimen. The decision to shorten the treatment duration for *C. koseri* bacteremia from the usual six weeks for non-surgical IE was based on the removal of the infection source and the absence of any residual infection in the surrounding heart

valve structures as observed during surgery. Three subsequent monthly follow-ups revealed persistently negative blood cultures, indicating the successful eradication of the infection. **Discussion:** Studies proposed shortening to 2 weeks for negative valve cultures revealed low incidence of relapse following surgical intervention, occurring only 0.8% of cases. Relapse, occurred in 2% of patients. No significant differences in relapse rates, 1-year recurrence, 1-year mortality, or postoperative complications between patients receiving antibiotics for more or less than two weeks. **Conclusion:** We report the successful management of a rare case of acute IE of the native mitral valve caused by *C. koseri* in an immunocompetent patient. Our treatment involved valve replacement and a shortened course of antimicrobial therapy.

### Keywords

Antimicrobial Treatment, *Citrobacter koseri*, Native Valve Infective Endocarditis, Mitral Valve Replacement

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## 1. Background

*Citrobacter koseri*, a Gram-negative, aerobic bacillus, is a ubiquitous organism found in water, soil, and the human gastrointestinal tract. While infections primarily affect immunocompromised individuals, we present a case of infective endocarditis (IE) caused by *C. koseri* in an immunocompetent patient. To our knowledge, this is the first documented case of *C. koseri* IE in the Philippines, while only nine (9) such cases have been reported worldwide. The patient underwent mitral valve replacement and received appropriate antimicrobial therapy. This case underscores the importance of considering *C. koseri* as a potential causative agent of IE, even in patients with seemingly robust immune systems.

## 2. Objective

To discuss a case of *C. koseri* IE successfully treated with mitral valve replacement and a shortened course of antimicrobial therapy.

## 3. Case Presentation

A 61-year-old male presented to the hospital with a three-week history of intermittent fever and an episode of delirium. The patient exhibited intermittent fever with temperatures ranging from 38°C to 39°C. Despite receiving a week of cefuroxime and azithromycin therapy, his symptoms persisted. He had no known comorbidities, reported no history of intravenous drug use, and tested negative for HIV.

On admission, the patient's vital signs were as follows: temperature 39°C, blood pressure 110/80 mmHg, heart rate 110 beats per minute, respiratory rate 22 cycles per minute, and oxygen saturation 97% on room air. Physical examination revealed dental caries in both upper and lower molars, oral thrush, and the absence

of skin rash, subconjunctival hemorrhage, Janeway lesions, and Osler's nodes. Pulmonary auscultation revealed bilateral crackles, with a greater intensity on the right lung. Cardiac auscultation revealed a regular heart rhythm with a soft second heart sound and a grade III/VI holosystolic murmur best heard at the fifth intercostal space along the midclavicular line. The abdomen was soft, non-distended, and non-tender without hepatosplenomegaly. Neurologic examination revealed orientation to time and place. Fundoscopic did not reveal Roth's spots.

Laboratory test results revealed anemia (12.5 g/dL), thrombocytopenia (99,000/mm<sup>3</sup>), leukocytosis (14,100/mm<sup>3</sup>), elevated alanine transaminase (50.70 U/L), and elevated procalcitonin (97.96 ng/mL). A chest X-ray showed opacities in both lower lung fields. Blood cultures were collected at the time of admission. The patient was initially diagnosed with acute infectious endocarditis with possible septic embolization, and community-acquired pneumonia. Empiric therapy was initiated with meropenem and vancomycin at meningitic doses.

Cranial computed tomography revealed enhancing lesions in the left frontal centrum semi-ovale and the cortical region of the right parietal lobe. A lumbar puncture was performed, revealing an elevated opening pressure suggestive of a central nervous system infection. However, cerebrospinal fluid chemistries and microbiological tests were unremarkable.

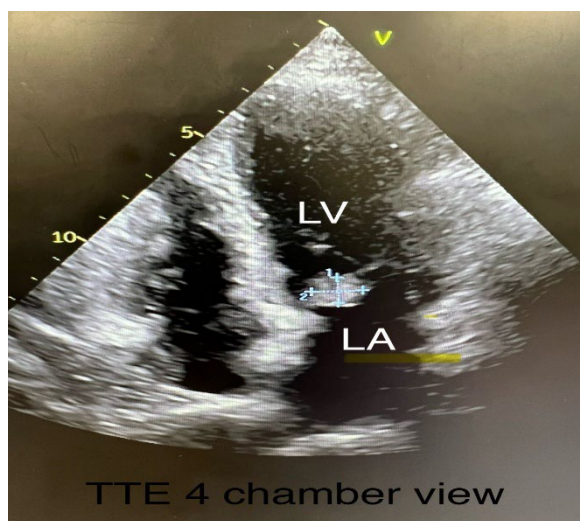
A transthoracic echocardiogram (TTE) noted a hyperdense echoluscent structure attached to the anterior mitral valve leaflet on the atrial side, measuring 1.2 cm and suggesting vegetation (**Figure 1**). Blood cultures from two sites returned positive for *C. koseri*. The blood isolate was resistant to ampicillin but susceptible to ureidopenicillin (piperacillin-tazobactam), high-generation cephalosporin (cefepime), carbapenems (ertapenem and meropenem), fluoroquinolones (ciprofloxacin and levofloxacin), and aminoglycosides (amikacin and gentamicin).



**Figure 1.** Transesophageal echocardiography showing large, mobile vegetation on the anterior mitral valve leaflet measuring 1.399 cm.

A transesophageal echocardiogram (TEE) confirmed the presence of a large,

mobile vegetation measuring 1.399 cm attached to the anterior mitral valve leaflet on the atrial side (**Figure 2**), as previously observed on the TTE. Based on these findings, the patient was diagnosed with acute IE of the native mitral valve caused by *C. koseri*. Given the patient's multiple risk factors for embolization, including a vegetation size greater than 10 mm, vegetation mobility, vegetation location on the anterior mitral valve leaflet, and the possibility of prior embolization, mitral valve replacement was recommended.



**Figure 2.** Four Chamber view Transthoracic echocardiography showing vegetation on anterior mitral valve leaflet measuring 1.2 cm.

During hospitalization, the patient developed right knee pain, characterized by warmth, slight swelling, and tenderness on examination. This was initially assessed as either septic or reactive arthritis. A point-of-care ultrasound revealed minimal effusion in the right knee, which was resolved with antimicrobial therapy.

While optimizing his condition for surgery, the patient developed nosocomial pneumonia. A chest X-ray revealed a progression of opacities in both lower lung fields. Vancomycin was replaced with tigecycline to address the potential for multidrug-resistant Gram-negative bacteria. Meropenem therapy was continued for the bacteremia. Repeat blood cultures performed 72 hours after initiating antibiotic treatment showed a resolution of bacteremia. The patient's pneumonia improved over three days.

Subsequently, the patient underwent mitral valve replacement, with intraoperative visualization of vegetations attached to the anterior mitral valve leaflet (**Figure 3**). There was no paravalvular extension of infection, annular abscess, or destructive penetrating lesion or fistula. Postoperatively, fever lysed, and inflammatory markers decreased (white blood cell count 7,100/mm<sup>3</sup> and procalcitonin 0.7 ng/mL). Repeat postoperative blood cultures remained sterile. Cultures of the excised anterior mitral valve leaflet were negative for bacterial growth, likely due to the targeted antimicrobial therapy administered before surgery.



**Figure 3.** Anterior mitral valve leaflet showing vegetation, myxohyaline degeneration and fibronopurulent inflammation. Posterior mitral valve leaflet showing myxohyaline degeneration.

Following a series of therapies, the patient was discharged with a three-week course of continuous intravenous meropenem therapy to complete the treatment regimen. The decision to shorten the treatment duration for *C. koseri* bacteremia from the usual six weeks for non-surgical IE was based on the removal of the infection source and the absence of any residual infection in the surrounding heart valve structures as observed during surgery. Three subsequent monthly follow-ups revealed persistently negative blood cultures, indicating the successful eradication of the infection

#### 4. Discussion

Citrobacter genus are motile, facultative, gram-negative, anaerobic bacteria in the family Enterobacterales. These organisms can be discovered in the water, soil, and digestive tract of both clinical samples of humans and animals [1]. Citrobacter species are considered low-virulence pathogens that cause illnesses less frequently [2]. Diabetes mellitus, congestive heart failure, hepatobiliary illness, cancer, or structural anomalies of the urinary system are risk factors for Citrobacter infections. Adult immunocompromised patients typically report infections, however, 11% of patients show no underlying illness [3]. *Citrobacter amalonaticus*, *Citrobacter diversus* (renamed as *C. koseri*), and *Citrobacter freundii* are three known species of Citrobacter that are pathogenic to humans [1].

Citrobacter is categorized as opportunistic and is frequently seen in infants and those with compromised immune states. Of the recorded cases, 46% are urinary infections, with respiratory tract infections at 16% and bacteremia at 16% [4]. Besides meningeal, respiratory, gastrointestinal, and soft-tissue infections, the bacteria can rarely cause IE. IE resulting from *C. koseri* is incredibly uncommon

which the literature only has a limited of published articles and studies. Non-HACEK Gram-negative bacilli IE is very rare, and the causing pathogen, *C. koseri*, is even less common. A study that investigated risk factors and outcomes of IE associated with Non-HACEK Gram-negative bacilli revealed that patients with implantable cardiac devices, urinary tract infections, and immunosuppression were at higher risk of IE, with a prevalence of Non-HACEK Gram-negative bacilli of 3.4% (58/1722 IE patients), 3 out of 58 patients infected by *C. koseri* [5]. Furthermore, prior research indicates that the biggest embolic risk is associated with anterior mitral valve vegetations (37%), as compared with posterior mitral vegetations (25%) and aortic vegetations (10%) [3].

The first documented case of *C. koseri* IE was reported in 1977, involving an aortic valve replacement. While rare, most documented cases (n = 9) have involved male patients aged 25 to 81, with antibiotic treatment and/or valve replacement being common interventions [4]. Based on our review of global literature, this is the first reported case of *C. koseri* IE in the Philippines. Of the nine documented cases worldwide, four (44%) required both antibiotic therapy and valve replacement, while one (11%) resulted in mortality. (Table 1)

**Table 1.** Summary of reported cases of *Citrobacter koseri* endocarditis [4].

Case	Year	Age	Sex	Risk Factor	Treatment	Prognosis
1	1977	43	Male	Not described	Cephalothin/gentamicin and aortic valve replacement	Alive
2	2000	51	Male	IV drug user	Ceftriaxone/gentamicin/vancomycin	Alive
3	2006	58	Male	Chronic Bronchitis	Cefotaxime/pefloxacin and mitral valve replacement	Dead
4	2009	30	Male	No comorbidities	Ceftriaxone/amikacin	Alive
5	2009	25	Male	Hemodialysis	Ciprofloxacin	Alive
6	2014	43	Male	IV drug user, Hepatitis C	Ticarcillin-clavulanate	Alive
7	2014	80	Female	Recurrent Pyelonephritis	Cefazolin/gentamicin and mitral valve replacement	Alive
8	2022	67	Male	Type 2 DM, Chronic kidney disease, atrial fibrillation, Septic shock of urinary origin	Ceftriaxone/cefuroxime	Alive
9	2023	81	Male	Testicular trauma with epididymitis	Cefazolin and mitral valve replacement	Alive

## 5. Treatment

By the 2023 ESC Guidelines for managing IE, early surgery and prolonged antibiotic therapy (6 weeks) are recommended for non-HACEK Gram-negative bacilli infections. Post-surgery, the recommended duration of antibiotic therapy for native valve endocarditis ranges from 7 days (with sterile valve cultures and completion of standard therapy) to 4 - 6 weeks (with positive intraoperative cultures) [6]. Some studies have proposed shortening this duration to 2 weeks for patients with negative valve cultures. A study of 358 patients with IE revealed a low incidence of relapse following surgical intervention, occurring in only 0.8% of cases. Despite

shortening the duration of postoperative antibiotic therapy, the authors observed no increase in the recurrence rate. These findings suggest that commonly cited factors for prolonging treatment, such as positive valve cultures or Gram stains, may not be essential. The authors conclude that a two-week course of antibiotics is generally sufficient for patients with negative valve cultures, and those nearing the completion of a standard treatment regimen can likely discontinue therapy without compromising outcomes [7]. Another study evaluated the impact of postoperative antibiotic duration on outcomes in 216 patients with IE who underwent heart valve surgery. The primary endpoint, IE relapse, occurred in only 2% of patients. There were no significant differences in relapse rates, 1-year recurrence, 1-year mortality, or postoperative complications between patients receiving antibiotics for more or less than two weeks. These findings suggest that a shorter duration of postoperative antibiotic therapy may be considered without compromising patient outcomes [6].

In our case, the patient underwent valve replacement and received 4 weeks of antibiotic therapy, including 1 week preoperatively and 3 weeks postoperatively. This extended duration was deemed necessary due to the development of possible septic embolization and septic arthritis during hospitalization. However, given the successful removal of the infection source and the absence of residual infection in the surrounding heart valve structures observed during surgery, a shortened postoperative course of 3 weeks (instead of 6 weeks) was deemed appropriate.

## 6. Conclusion

We report the successful management of a rare case of acute IE of the native mitral valve caused by *C. koseri* in an immunocompetent patient. Our treatment involved valve replacement and a shortened course of antimicrobial therapy.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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