


# Successful Resolution of Early-Onset Prosthetic Valve Endocarditis Associated With Extended Spectrum $\beta$ -Lactamases Producing *Escherichia coli* With Medical Management

Journal of Investigative Medicine High  
Impact Case Reports  
Volume 8: 1–4  
© 2020 American Federation for  
Medical Research  
DOI: 10.1177/2324709620965337  
journals.sagepub.com/home/hic  


Umaima Dhamrah, MD<sup>1</sup> , Keely Johnson, MD<sup>1</sup>,  
Aisha Amin, MD<sup>1</sup>, and Maurice Policar, MD<sup>1</sup>

## Abstract

A 74-year-old male with a recent bioprosthetic mitral valve placement presented with dyspnea, chills, and palpitations. Blood cultures on admission grew extended spectrum  $\beta$ -lactamase *Escherichia coli*. Transthoracic echocardiogram and transesophageal echocardiography were negative for valvular vegetations, but given the recent history of mitral valve replacement and difficulty visualizing valvular vegetations in prosthetic valve, we initiated treatment of our patient with antibiotics for 6 weeks. Repeat blood cultures showed clearance of the organism and on follow-up, and the patient had no signs of recurrence of infection.

## Keywords

infective endocarditis, ESBL, *E coli*, echocardiogram, TTE, TEE, empiric treatment, prosthetic valve

## Introduction

*Escherichia coli* is a rare cause of infective endocarditis (IE), associated with high mortality when left untreated. *E coli* is the causative microorganism in approximately 0.51% of cases of IE.<sup>1</sup> The global incidence of early-onset prosthetic valve endocarditis (EO-PVE) is 1.4% to 3.1% within the first year after valve replacement.<sup>2,3</sup> EO-PVE within the first year are directly related to the surgical procedure and perioperative period.<sup>2</sup>

We herein report a unique case of EO-PVE caused by extended spectrum  $\beta$ -lactamase (ESBL) *E Coli* in a patient with recent mitral valve replacement, 5 weeks prior to his presentation. Our patient had no valvular vegetations on echocardiogram; however, due to high suspicion, we elected for treatment with 6 weeks of antibiotics with subsequent clearance of cultures.

## Case

A 74-year-old male with a past medical history of hypertension, coronary artery bypass graft and recent mitral valve replacement with a bioprosthetic valve for severe mitral regurgitation with calcification of leaflets and posterior annulus, presented to the emergency room complaining of

dyspnea, palpitations, and chills at home for 1 day. The patient also reported having noticed lower extremity edema for a few days prior to admission. He denied cough, chest pain, orthopnea, abdominal pain, or dysuria.

On physical examination, the patient displayed no peripheral stigmata of IE, no murmurs were appreciated. The patient had decreased breath sounds up till the middle lung zones, and 2+ pitting lower extremity edema. On initial laboratory tests, his white blood cells count was 18.1, with 97.9% neutrophils, 8% bands, and a lactate of 3.7. Other significant laboratory tests included troponin peak of 0.067, and a pro-brain natriuretic peptide of 2636. Initial chest X-ray showed mild pulmonary congestion and mild symmetrical bilateral pleural effusions. One of the 2 blood cultures collected at admission grew ESBL *E Coli* (Figure 1). Biliary tract and urinary sources were considered

<sup>1</sup>Icahn School of Medicine at Mount Sinai, Elmhurst Hospital Center, Elmhurst, NY, USA

Received June 21, 2020. Revised September 10, 2020. Accepted September 13, 2020.

## Corresponding Author:

Umaima Dhamrah, MD, Icahn School of Medicine at Mount Sinai, Elmhurst Hospital Center, 79-01 Broadway, Elmhurst, NY 11373, USA.  
Email: dhamrahumaima@gmail.com



Susceptibility		Escherichia Coli ESBL MIC	
Amikacin	<=2	Sensitive	
Ampicillin	>=32	Resistant	
Ampicillin/Sulbactam	>=32	Resistant	
Cefazolin	>=64	Resistant	
Cefepime	>=64	Resistant	
Ceftazidime	>=64	Resistant	
Ceftriaxone	>=64	Resistant	
Ciprofloxacin	>=4	Resistant	
ESBL		Positive	
Gentamicin	<=1	Sensitive	
Imipenem	<=0.25	Sensitive	
Levofloxacin	>=8	Resistant	

**Figure 1.** Susceptibility testing in extended spectrum  $\beta$ -lactamase (ESBL) *Escherichia coli* bacteremia.

unlikely. While urine studies grew <1000 CFU (colony-forming unit) gram-negative rods and *Staphylococcus* species, urinalysis was negative for nitrites and leukocytes, thus culture results were most consistent with likely contaminants. Liver function test remained only mildly elevated, with aspartate transaminase 64 and alanine aminotransferase 89, throughout hospital admission. Given ESBL *E coli* positive blood cultures 6 weeks after valve replacement, EO-PVE in setting of environmental contamination was suspected as the most likely source. Per operative report, the patient received standard preoperative and postoperative prophylactic antimicrobial coverage. Since valve-replacement occurred in an outside facility, further hospital investigations to determine the source of environmental contamination were not possible. At time of valve replacement, left and right ventricular function were preserved and cardiac catheterization showed normal coronary arteries. Transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE) on admission at our facility showed diffusely hypokinetic wall motion with left ventricular ejection fraction 40%, with no mitral regurgitation; however, no signs of valve vegetation were visualized. As both TTE and TEE were negative for valvular vegetations, cardiothoracic surgery was not consulted.

Given the recent mitral bioprosthetic valve replacement, we initiated empiric treatment of our patient based on high clinical suspicion for IE. Blood cultures were sensitive to amikacin and imipenem. Since *Pseudomonas aeruginosa* and *Enterococcus* spp coverage was not indicated, and the patient was to be discharged on outpatient intravenous antimicrobial therapy, we chose to narrow to treatment with amikacin and ertapenem for 6 weeks. The patient was followed by ENT, while on amikacin

**Table 1.** Valvular Sites of Infection of *Escherichia coli*.

Mitral valve	58%
Aortic valve	5% to 37%
Pulmonic valve	11% to 17%
Tricuspid valve	17%

with weekly basic metabolic panel to monitor creatinine clearance. Repeat audiogram was ordered; however, the patient failed to follow-up. Repeat cultures were negative by day 6 of antibiotics. The patient reported subjective worsening of hearing loss at 5 weeks concerning for aminoglycoside toxicity and amikacin was discontinued. The patient was continued on ertapenem only to complete the course of antibiotic treatment. Blood cultures at 5 weeks were negative. Repeat echocardiogram 1 month later was unchanged from prior. Follow-up echocardiogram at the completion of antimicrobial therapy to establish cure or new baseline for comparison for our patient remains undetermined as attempts to discuss results of follow-up with outside cardiologist were unsuccessful.

On follow-up with the patient, 10 months later, there were no signs of recurrence of infection.

## Discussion

Gram-positive bacteria cause 80% of all IE cases; however, gram-negative bacteria are also causative agents<sup>4</sup> with *E coli* causing 44% of all gram-negative bacteremia.<sup>5</sup> With the exception of the HACEK organisms (ie, *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella*),

**Table 2.** Duke Criteria.

---

1.	Blood culture positive for IE <ul style="list-style-type: none"> <li>a. Typical microorganisms consistent with IE from 2 separate blood culture           <ul style="list-style-type: none"> <li>• Viridans streptococci, <i>Streptococcus bovis</i>, HACEK group, <i>Staphylococcus aureus</i>; or</li> <li>• Community-acquired enterococci, in the absence of a primary focus; or</li> </ul> </li> <li>b. Microorganism consistent with IE from persistently positive blood cultures, defined as follows:           <ul style="list-style-type: none"> <li>• At least 2 positive cultures of blood samples drawn &gt;12 hours apart; or</li> <li>• All of 3 or a majority of <math>\geq 4</math> separate cultures of blood (with first and last sample drawn at least 1 hour apart)</li> </ul> </li> <li>c. Single positive blood culture for <i>Coxiella burnetii</i> or antiphase I IgG antibody titer &gt;1&gt;800</li> </ul>
2.	Evidence of endocardial involvement <ul style="list-style-type: none"> <li>a. Echocardiogram positive for IE (TEE recommended in patient with prosthetic valves; rated at least “possible” IE by clinical criteria or complicated IE (paravalvular abscess); TTE as first test in other patients), defined as follows:           <ul style="list-style-type: none"> <li>• Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or</li> <li>• Abscess; or</li> <li>• New partial dehiscence of prosthetic valve</li> </ul> </li> <li>b. New valvular regurgitation (worsening or changing of preexisting murmur not sufficient)</li> </ul>
Minor criteria	
<ul style="list-style-type: none"> <li>• Predisposition, predisposing heart condition, or injection drug use</li> <li>• Fever, temperature &gt;38 °C</li> <li>• Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway’s lesions</li> <li>• Immunologic phenomena: glomerulonephritis, Osler’s nodes, Roth’s spots, and rheumatoid factor</li> <li>• Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE</li> </ul>	

---

Abbreviations: IE, infective endocarditis; HACEK, *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella*; IgG, immunoglobulin G; TEE, transesophageal echocardiogram; TTE, transthoracic echocardiogram.

*E coli* is the most frequent cause of IE due to gram-negative bacteria. Implanted endovascular devices are frequently associated with non-HACEK gram-negative bacillus endocarditis compared with other causes of endocarditis.<sup>1</sup>

Mitral valve is the most common site of infection (Table 1).<sup>6,7</sup> Mortality rates of 53% to 65% have been reported in patients with *E coli* endocarditis.<sup>6,7</sup> Although *E coli* does not stick to native heart valves as easily as staphylococci and streptococci,<sup>8</sup> it does cause PVE and has been reported with a frequency as high as 19%, in 7 of 37 cases of all cause endocarditis.<sup>6</sup>

Some of the risk factors associated with infections caused by ESBL producing organisms are advanced age, female gender, diabetes mellitus, prolonged hospital stay, prior exposure to cephalosporins, quinolones, and 3 or more courses of antibiotic therapy in the preceding year.<sup>1</sup> The mortality rate of *E coli* endocarditis is higher than that of endocarditis due to the HACEK-group gram-negative bacteria<sup>6</sup> that may correlate with *E coli* bacteremia being erroneously attributed to more benign sources, like urosepsis, rather than being recognized initially as an indication of endocarditis. A delay in correct diagnosis can lead to a delay in consideration of early valve replacement and lack of a prolonged course of antibiotic therapy in appropriate cases that may lead to complications like intracardiac abscess, sepsis, and in hospital mortality.<sup>9,10</sup>

Patients with a prosthetic valve have a higher risk of IE and are more likely to develop complications than patients with native valves.<sup>11</sup> PVE accounts for 15% of all

endocarditis cases. It is divided into early endocarditis, which is most often defined as occurring <1 year from implant surgery, and late endocarditis, which occurs more than 1 year after implantation.<sup>2</sup> Vegetations are difficult to visualize in patients with preexisting lesions like mitral valve prolapse, prosthetic valves, very small vegetations (<2 mm), and in cases where vegetations are not yet present.

The sensitivity of TTE for detection of valve vegetations is between 40% and 63% and that of TEE ranges from 90% to 100%. Regardless, diagnosing IE is particularly challenging in patients with prosthetic heart valves, even with TEE.<sup>11</sup> Similarly, presence of prosthetic valves makes it difficult to identify small abscesses.<sup>12</sup> TTE and TEE may be repeated in 7 to 10 days in the cases with initial negative examination.<sup>11</sup> It is, therefore, important to have a high index of suspicion and low threshold to investigate these high-risk groups.

Duke criteria has been used as a criteria for the diagnosis of IE<sup>13</sup> (Table 2). While the Duke criteria has a high sensitivity and specificity (about 80%), clinical judgement remains essential in high-risk cases when the infection involves a prosthetic valve, IE of right heart, and when blood cultures are negative. In these cases of PVE the sensitivity of Duke’s criteria is diminished with sensitivity reduced to 67%.<sup>3,14,15</sup>

In situations in which the primary location of infection is not identified in either the urinary tract, or the biliary system, we suggest that it is important to consider endocarditis as a primary source in patients with a history of valvular replacement and ESBL *E Coli*-positive blood cultures. An individualized

approach that considers infective organism, presence of valvular vegetations, heart failure, and prosthetic valve dysfunction on presentation may assist with identifying cases in which medical management can be successful in full eradication of ESBL *E Coli* EO-PVE. As TTE and TEE may be inadequate for diagnosis of endocarditis in patients with prosthetic valves, it is critical to carefully choose broad-spectrum empiric antibiotic therapy that carefully takes into consideration the antibiotic resistance of the communities in which the organism was acquired. The American Heart Association recommends a 6 weeks antibiotic therapy with a combination of  $\beta$ -lactams and either an aminoglycoside or fluoroquinolone in patients with non-HACEK gram-negative endocarditis.<sup>9</sup> ESBL-positive cultures confer resistance to third- and fourth-generation cephalosporins, monobactams, fluoroquinolones, tetracyclines, and aminoglycosides.<sup>10</sup> In areas where there is high prevalence of carbapenem resistance, it may be preferable to treat primarily with drugs that have otherwise widely fallen out of use, such as aminoglycosides, in appropriate cases.

## Limitations

Our diagnosis is uncertain. We did not meet criteria for PVE. Only 1 of 2 sets of blood cultures were positive. IE is usually associated with a continuous bacteremia. No other source of infection was found, but it is possible that a gastrointestinal source was undiagnosed, or a pneumonia could not be distinguished from radiologic changes due to congestion from heart failure. There was no symptomatology to support pneumonia.

Regardless, bacteremia from any source in a patient with a prosthetic valve is a high risk for PVE. Given the highly resistant nature of the organism involved and the repercussions of inadequately treating PVE, we thought it prudent to treat aggressively.

## Authors' Note

This article has been presented as an abstract and poster in SGIM 2020 On-Demand Virtual Conference in June, 2020.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

## Ethics Approval

Institutional review board approval is not required for case reports at our institution.

## Informed Consent

Informed consent for patient information to be published in this article was not obtained because our institution does not require informed consent for individual case reports.

## ORCID iD

Umama Dhamrah  <https://orcid.org/0000-0003-3203-9797>

## References

- Morpeth S, Murdoch D, Cabell CH, et al. Non-HACEK gram-negative bacillus endocarditis. *Ann Intern Med.* 2007;147:829-835.
- Gordon SM, Serkey JM, Longworth DL, Lytle BW, Cosgrove DM 3rd. Early onset prosthetic valve endocarditis: the Cleveland Clinic experience 1992-1997. *Ann Thorac Surg.* 2000;69:1388-1392.
- López J, Revilla A, Vilacosta I, et al. Definition, clinical profile, microbiological spectrum, and prognostic factors of early-onset prosthetic valve endocarditis. *Eur Heart J.* 2007;28:760-765.
- Bennett JE, Dolin R, Blaser MJ. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases.* Elsevier; 2014:3697.
- Hernandez C, Feher C, Soriano A, et al. Clinical characteristics and outcome of elderly patients with community-onset bacteremia. *J Infect.* 2014;70:135-143.
- Branger S, Casalta JP, Habib G, Collard F, Raoult D. *Escherichia coli* endocarditis: seven new cases in adults and review of the literature. *Eur J Clin Microbiol Infect Dis.* 2005;24:537-541.
- Akuzawa N, Kurabayashi M. Native valve endocarditis due to *Escherichia coli* infection: a case report and review of the literature. *BMC Cardiovasc Disord.* 2018;18:195.
- Tsutsumi T, Hiraoka E, Kanazawa K, Akita H, Eron LJ. Diagnosis of *E. coli* tricuspid valve endocarditis: a case report. *Hawaii Med J.* 2010;69:286-288.
- Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. *Circulation.* 2015;132:1435-1486.
- Livermore DM, Woodford N. The beta-lactamase threat in *Enterobacteriaceae*, *Pseudomonas* and *Acinetobacter*. *Trends Microbiol.* 2006;14:413-420.
- Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. *Eur Heart J.* 2009;30:2369-2413.
- Hill EE, Herijgers P, Claus P, Vanderschueren S, Peetermans WE, Herregods MC. Abscess in infective endocarditis: the value of transesophageal echocardiography and outcome: a 5-year study. *Am Heart J.* 2007;154:923-928.
- Topan A, Carstina D, Slavcovici A, Rancea R, Capalneau R, Lupse M. Assessment of the Duke criteria for the diagnosis of infective endocarditis after twenty-years. An analysis of 241 cases. *Clujul Med.* 2015;88:321-326.
- Prendergast BD. Diagnostic criteria and problems in infective endocarditis. *Heart.* 2004;90:611-613.
- Pérez-Vázquez A, Fariñas MC, García-Palomo JD, Bernal JM, Revuelta JM, González-Macías J. Evaluation of the Duke criteria in 93 episodes of prosthetic valve endocarditis: could sensitivity be improved? *Arch Intern Med.* 2000;160:1185-1191.