



Case report

Escherichia coli prosthetic valve endocarditis from a non-genitourinary source

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ARTICLE INFO

Article history:

Received 22 September 2021

Received in revised form 3 November 2021

Accepted 4 November 2021

Available online xxxxx

Keywords:

Infective endocarditis

Prosthetic valve

Escherichia coli

ABSTRACT

Escherichia coli (*E. coli*) is a rare cause of infective endocarditis due to its lack of traditional virulence factors that promote endocardial adherence. Previous case reports of *E. coli* infective endocarditis demonstrate specific risk factors to include advanced age over 70, female sex, diabetes, immunosuppression, and intravascular or cardiac devices. Antecedent genitourinary infection is the most common source. We present a case of a 55-year-old Honduran man with a recent bioprosthetic mitral valve replacement and tricuspid valve repair who presented with one month of subjective fevers, night sweats, anorexia, and significant weight loss. After extensive work-up, the patient was diagnosed with *E. coli* infective endocarditis secondary to *E. coli* growth in blood cultures and a transesophageal echocardiogram (TEE) revealing a vegetation on his prosthetic mitral valve. An indolent gastrointestinal source was suspected to be the source of infection with imaging only notable for mild periappendiceal stranding concerning for a possible site of antecedent inflammation. He was treated with a 6-week course of ceftriaxone and gentamicin inpatient and then discharged on trimethoprim-sulfamethoxazole suppressive therapy with serial echocardiographic follow-up given the persistent small vegetation on repeat echocardiogram. Our case report and review of ten recent cases of prosthetic valve endocarditis described in the literature illustrates several common features of the epidemiology, presentation, and management of *E. coli* prosthetic valve endocarditis including more commonly reported non-genitourinary sources of bacteremia, a trend towards more frequent surgical interventions, and a declining mortality rate.

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Introduction

Infective endocarditis (IE) is a life-threatening infection of the endocardial surface of the heart or heart valves which can result in severe cardiac dysfunction. Most cases are caused by gram positive organisms or fastidious gram negative oral flora known as the

"HACEK organisms" owing to the numerous virulence factors these pathogens possess aiding endocardial adherence [1,2]. *Escherichia coli*, a gram-negative bacillus member of the *Enterobacteriaceae* family, typically lacks these traditional virulence factors and is subsequently an infrequent cause of IE accounting for only 0.5% of cases in a large international cohort [3,4]. While there are a variety of sources of initial infection, an antecedent infection in the urinary tract is often identified as the source of initial bacteremia that seeds the heart valves [4,5]. In this report we present a unique case of *E. coli* prosthetic mitral valve endocarditis in a 55-year-old man seeded from a non-genitourinary source. We subsequently review 10 cases of *E. coli* prosthetic valve endocarditis (PVE) found in the literature over the past 20 years and provide a characterization of this illness.

Case presentation

A 55-year-old Honduran man with a past medical history of non-ischemic cardiomyopathy due to valvular heart disease with

Abbreviations: AI, Aortic insufficiency; AMI, Acute myocardial infarction; AMK, Amikacin; AMP, Ampicillin; AV, Aortic valve; AVR, Aortic valve replacement; CEF, Cefalexin; CIP, Ciprofloxacin; CTX, Ceftriaxone; *E. coli*, *Escherichia coli*; EF, Ejection Fraction; GENT, Gentamicin; GI, Gastrointestinal; GU, Genitourinary; HACEK, *Haemophilus species*, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*; IE, Infective Endocarditis; IMP, Imipenem; M, Man; MR, Mitral regurgitation; MV, Mitral valve; MVR, Mitral valve replacement; OFL, Ofloxacin; PVE, Prosthetic valve endocarditis; SD, Standard deviation; SUL, Sulbactam; TV, Tricuspid valve; Unk, Unknown; UTI, Urinary tract infections; W, Woman; WMA, Wall motion abnormalities *Infective endocarditis*

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associated combined heart failure (ejection fraction 40%, stage III diastolic dysfunction), a recent bioprosthetic mitral valve replacement with tricuspid valve repair (2 months prior to admission), and paroxysmal atrial fibrillation presented to our hospital with 3 weeks of subjective fevers, night sweats, 30-pound weight loss, fatigue, and anorexia. One month prior to this presentation, the patient was briefly admitted following his valve replacement surgery with a day of watery diarrhea and was found to be in septic shock due to *E. coli* bacteremia of uncertain source. Evaluation during this admission included an unremarkable urinalysis and urine cultures and CT imaging only notable for distention and mild dilation of the small bowel suggestive of possible enteritis. Stool studies were not obtained given the self-limited nature of his antecedent diarrheal illness, but serum *Strongyloides* serologic testing was notably negative at the time. After a brief parenteral antimicrobials course, he was instructed to complete a two-week course of oral cefpodoxime 200 mg q12h upon discharge for transient bacteremia from a presumed self-limited gastrointestinal source.

He did well clinically for one week after discharge before developing subjective fevers with generalized myalgias despite his outpatient cefpodoxime course. Over the following 3 weeks the patient progressively declined with more frequent subjective fevers, night sweats, malaise, anorexia with weight loss, and abdominal fullness further prompting another presentation to the emergency department. He denied sternal wound pain or drainage and a thorough review of systems for other localizing infectious symptoms was otherwise negative.

On admission, vital signs were notable for a temperature of 38.8 °C (101.8 °F), blood pressure 91/62 mm Hg, heart rate 84 beats per minute, respiratory rate 21 breaths per minute, and oxygen saturation 100% on room air. Physical examination revealed an irregularly irregular heartbeat without murmur and an unremarkable lung exam. His abdomen was soft, nondistended, nontender to palpation, and no organomegaly was noted. No distal extremity edema or distal embolic phenomena were noted on skin exam. Notably, a stage 2 sacral wound that had developed following his valve surgery had healed completely since his prior admission. Laboratory tests were significant for a leukocytosis with a white blood cell count of 14000 (normal 4500–11000 cells/ μ l), anemia with a hemoglobin of 9.4 (normal 13.5–17.5 gm/dL), and normal kidney and liver function on complete metabolic panel. Inflammatory markers were elevated with a sedimentation rate of 119 mm/hour (normal 0–20 mm/hr). Urinalysis and culture were again unremarkable.

Chest radiograph showed no evidence of acute cardiopulmonary disease, and an initial transthoracic echocardiogram showed no obvious vegetations or compromise of his prosthetic valve. The patient was started on broad spectrum antimicrobials with intravenous vancomycin 1 g q12h and cefepime 2 g IV q8h at the time of admission. Antibiotics were quickly narrowed to cefepime alone after admission blood cultures ultimately grew gram-negative rods in 4/4 collection tubes which later speciated as *Escherichia coli*. He was transitioned to ceftriaxone 2 g IV q24h based on sensitivity data, but blood cultures remained persistently positive on hospital day 2 and 3 raising concern for an endovascular nidus of infection. Transesophageal echocardiogram was obtained on hospital day 5 which revealed a small 3 mm mobile, filamentous vegetation on the anterior cusp of the prosthetic mitral valve without significant valvular compromise. As a result, he met Duke criteria for diagnosis of infective endocarditis by fulfilling one major criterion (TEE demonstrating a vegetation) and three minor clinical criteria (persistent fevers, predisposing cardiac condition, and persistently positive cultures.) [6].

Antimicrobial therapy was tailored to combination therapy with ongoing ceftriaxone 2 g IV q24h and gentamicin 5 mg/kg IV q24h which was adjusted continually based on levels of accumulation and

changes in renal function. He continued to improve clinically, and blood cultures demonstrated complete clearance on hospital day 5. Given that the patient lacked evidence of an antecedent urinary tract infection as the source of his recurrent bacteremia, additional imaging was obtained to exclude a secondary source or nidus of infection. This included CT of the chest, abdomen, and pelvis to exclude an indolent abscess and doppler ultrasounds of the extremities and portal vasculature to exclude septic thrombophlebitis. An MRI of the full spine was also performed to exclude osteomyelitis/discitis given his prior sacral wound during his previous hospitalization. Imaging studies were only notable for mild periappendiceal stranding concerning for a possible site of antecedent inflammation as the source of his recurrent *E.coli* bacteremia. Given a benign abdominal exam, surgical consultants did not feel he met criteria for acute appendicitis and declined intervention. Neither a colonoscopy nor capsule endoscopy were performed during his inpatient stay owing to limitations on endoscopic procedures performed during a concurrent coronavirus pandemic surge. Given the patient's rapid clinical improvement on tailored antimicrobial coverage, cardiothoracic surgery concluded that the risks of redo-valve replacement outweighed the benefits as there were no significant valvular defects noted on echocardiogram.

The patient subsequently completed a six-week course of combination antimicrobial therapy with appropriate levels of gentamicin and no adverse sequelae of therapy. Repeat echocardiogram showed a largely unchanged small mobile vegetation on the anterior cusp of the prosthetic mitral valve without valvular compromise. He was reassessed by cardiothoracic surgery who again recommended conservative management with chronic oral suppression and additional echocardiographic follow-up given his overall clinical improvement without significant valvular compromise on serial echocardiograms. He was subsequently transitioned to suppressive therapy with trimethoprim-sulfamethoxazole given the presence of continued vegetation on his prosthetic valve with plans for withdrawal after a distant repeat echocardiogram at 6 months of follow-up. The patient was reevaluated several weeks post-discharge and remained clinically well. Unfortunately, he was not seen again in follow-up at our clinic since he returned to his home country of Honduras for continuity of care.

Discussion

While both native and prosthetic valve IE due to *E.coli* has been described as a rare entity, previous studies have characterized *E. coli* IE as frequently stemming from nosocomial origin and more likely related to an antecedent genitourinary infection [3,8]. These studies have also demonstrated a greater association with endovascular devices for cases of *E. coli* IE with PVE accounting for 8% of all cases before the year 2000 [8]. Since the year 2000, however, the share of *E.coli* IE cases involving prosthetic valves has significantly increased with PVE now accounting for 33% of 27 reported cases of *E.coli* IE described in a recent review of the literature [7]. This increase in prosthesis infection is likely a reflection of the increasing incidence of valve surgery and cardiac device implantation over this same time period [1,2].

Previously characterized risk factors for the development of *E.coli* IE include advanced age over 70, female sex, diabetes, immunosuppression, and implanted intravascular or cardiac devices [5,7–8]. Table 1 illustrates the clinical characteristics of the 10 cases of *E.coli* PVE described in the literature over the last 20 years which includes our own case [8–11]. Although antecedent urinary tract infection preceded the development of *E.coli* PVE in 40% of these reviewed cases, we found that documented gastrointestinal infection or pathology preceded the diagnosis of PVE in 50% of cases. This trend reflects a notable increase in recognition of this organ system

Table 1
Characteristics of *E.coli* prosthetic valve endocarditis cases.

Case #	Author	Year	Age/Sex	Medical History	Source	Valve Infected	Echo Findings	Emboic Events	Antibiotics	Surgery	Outcome
1	Branger (8)	2005	60yo W	Colonic polyposis and prior AVR	GI source	Prosthetic AV	AI with cusp rupture	No	CEF + CIP x6wks	Yes	Alive
2	Branger (8)	2005	76yo M	Kidney cancer and prior MVR	GI source	Prosthetic MV	Vegetation	No	CIP x 6wks	No	Alive
3	Branger (8)	2005	66yo W	Prior MVR	GU source	Prosthetic MV	Vegetation + valve ring abscess	No	IMP + GENT x2wks -> CTX x 4wks	Yes	Alive
4	Branger (8)	2005	76yo W	Colonic polyposis, recurrent UTI's, and prior MVR	GU source	Prosthetic MV	WMA/AMI	Unknown	Unknown	Unknown	Unknown
5	Modi (11)	2011	62yo W	Prior MVR	Unknown	Prosthetic MV	Vegetation + mild MR	No	IMP x 6wks	No	Alive
6	Senel (10)	2012	60yo M	Prior AVR, recent hemorrhoi-dectomy, active enteritis	GI source	Prosthetic AV	Valve ring abscess	No	AMP/SUL + GENT x 6wks	Yes	Alive
7	Loubet (11)	2015	82yo Unk	Prior AVR	GU source	Prosthetic AV	Valve ring abscess	No	Unknown + AVR	Yes	Alive
8	Loubet (11)	2015	74yo Unk	Prior MVR	GI source	Prosthetic MV	Valve ring abscess	Yes	CTX + AMK	No	Alive
9	Loubet (11)	2015	74yo Unk	Prior AVR	GU source	Prosthetic AV	Valve ring abscess	No	CTX + OFL x 6wks	No	Death
10	Quiring	2021	55yo M	Prior MVR and TV repair	GI source	Prosthetic MV	Vegetation	No	CTX + GENT x 4wks	No	Alive
Total	N/A	N/A	68.5 yrs (SD = 8.5 yrs)	30% chronic GI pathology; 20% chronic GU pathology	50% GI, 40% GU, 10% unknown source	60% MVR, 40% AVR	50% valve ring abscess	10% embolic events	Heterogenous; combination 60%	40% surgery	80% alive, 10% death, 10% unknown

as a source of *E.coli* PVE [7]. Notably the mitral valve remained the most commonly affected valve in PVE cases and distant embolic events were rare occurring in only 10% of cases. Valve ring abscess was a commonly described complication in these PVE cases reported in 50% of patients [8–11]. Although exact antimicrobial regimens remain heterogeneous among individual cases, combination therapy is the standard treatment for PVE and was utilized in 60% of reviewed cases [8–11]. Surgical intervention was performed frequently in 40% of cases owing to the increasing frequency of intracardiac abscess in PVE cases [8–11]. Despite the inherent risks of combination antimicrobial therapy and surgery, early mortality is encouragingly lower at 10% compared to the reported 21% of overall cases of *E. coli* infective endocarditis reviewed by Akuzawa and colleagues [7].

Our case described in this report illustrates several common epidemiological, presentation, and management trends of *E.coli* PVE. In particular, our patient possessed a major risk factor for the development of *E.coli* IE by nature of having an implanted prosthetic mitral valve. In contrast to previously described risk factors, our patient did not have an antecedent genitourinary infection as the source of his initial bacteremia. Although there was no concrete evidence for a gastrointestinal source or nidus of infection, serial imaging revealed small bowel and periappendiceal stranding which suggests sites of inflammation that may have resulted in translocation of *E.coli* into the bloodstream and initial seeding of his valve. Serum *Strongyloides* serologic testing was negative and unfortunately could not provide a unifying diagnosis to explain his patchy intestinal stranding and transient episodes of enteric bacteremia. Given the constraints of the pandemic on our local medical system and the patient's preordained return to his home country within several months of initial treatment, we could not further evaluate for a nidus of infection within the gastrointestinal tract with endoscopy. Regardless of the exact source of the initial infection, his presentation illustrates the emerging trend that the genitourinary system is no longer the only anticipated source of bacteremia in *E.coli* PVE cases. The patient did not have the feared complication of valve ring abscess requiring redo-valve replacement given his rather prompt initial presentation to the healthcare system and early, although intermittent, administration of antimicrobials. Consistent with the standard of care, he received combination antimicrobial therapy and did clinically well following his treatment course.

Conclusion

Although *E. coli* endocarditis is a rare condition, it is necessary to ensure a prompt diagnosis and timely intervention due to the high mortality rate. With the relatively high incidence of *E.coli* bacteremia in hospitalized patients, practitioners should strongly consider including echocardiography in the diagnostic evaluation of those patients with persistent or relapsed *E.coli* bacteremia – particularly those patients with prosthetic valve replacements. Although urinary tract infections historically have been described as the most common source of *E.coli* bacteremia, our case and a recent literature review suggests an increasing prevalence of non-genitourinary sources of *E.coli* PVE. Therefore, clinicians should consider detailed evaluation of systems beyond the urinary tract when evaluating potential *E. coli* PVE cases.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for profit sectors.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

Robert Quiring: Investigation, Writing – original draft, Writing – review & editing. **Victoria Burke:** Supervision, investigation, Writing – original draft, Writing – review & editing.

Acknowledgments

Special thanks to LSUHSC Library and Reference Librarian, Kathryn Kerdolff, for her assistance in conducting a thorough literature review.

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