Enterobacter Cloacae Device Endocarditis: Case Report, Scoping Study, and Guidelines Review

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ABSTRACT
While traditionally an infection of the endocardial surface of heart valves, infective endocarditis (IE), can atypically present as infection of cardiac implantable electronic devices (CIED), including permanent pacemakers (PPM) or automatic implantable cardioverter-defibrillators (AICD). CIED endocarditis, similar to valvular IE, is generally caused by Gram-positive organisms such as Staphylococcus spp., most frequently S. Aureus, but is rarely caused by gram-negative bacteria, both HACEK and non-HACEK species. We present the case of Enterobacter cloacae CIED endocarditis. We also present a scoping study of previous case reports and case series highlighting the risk factors, surgical interventions, and mortality outcomes associated with E. Cloacae endocarditis. We also discuss the current guidelines and recommendations on antibiotic therapies for non-HACEK Gram-negative endocarditis and surgical management of infected CIED extraction and replacement.

Keywords
Enterobacter cloacae, Cardiac Implantable Electronic Device, Infective Endocarditis.

Introduction
Infective endocarditis (IE), the microbial infection of the endocardium generally affecting cardiac valves, is classified based on diagnostic studies (definite or possible), anatomical involvement (left-sided, involving the mitral and/or aortic valve vs. right-sided, involving the tricuspid and/or pulmonic valve), microbiology (bacterial, fungal), and valve nativity or prostheses [1-3]. Suspected IE is evaluated as definite or possible based on the combination of echocardiographic, microbiologic, laboratory, and physical findings making up the Duke and Modified Duke Criteria [2,4]. Left-sided IE (LSIE) is more common than right-sided IE (RSIE) and affects diverse patient populations with traditional risk factors such as underlying valvular or structural heart disease with or without previous surgery or prosthesis, history of endocarditis, and predisposing clinical characteristics and comorbidities such as advanced age and immunosuppressive populations such as malignancy, cirrhosis, chronic kidney disease, and diabetes mellitus [1,5,6]. The microorganisms most commonly isolated in IE are Staphylococcus species, primarily Staph. aureus, and the HACEK group (Haemophilus spp., Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella spp., Kingella kingae) of Gram-negative rods, and the high rates and associations of these bacteria with IE has resulted in the specific incorporation of these organisms in the microbiologic parameters of the Duke Criteria [2,7].

In parallel to but significantly rarer than IE affecting cardiac valves is cardiac implantable electronic device (CIED) endocarditis, infection of implanted permanent pacemakers (PPM) or automatic implantable cardioverter-defibrillator (AICD) involving any component of the device, including the intracardiac or large blood vessel region of the electrode lead, the tissue ‘tunnel’ through which the lead travels prior to entering the blood vessel, or the subcutaneous ‘pocket’ device electrical generator [8,9]. CIED endocarditis can result from direct primary infection of any region of the device, most commonly the intracardiac electrode lead, or from secondary seeding in the setting of bacteremia and sepsis.
of a distant site, and is most frequently caused by Gram-positive
organisms, specifically Staph. aureus and Staph.epidermidis,
with significantly less cases caused by gram negative rods or
Streptococcus species [8-11].

In comparison to the usual causative organisms of bacteremia and
both IE and CIED endocarditis, Enterobacter spp., specifically
Enterobacter cloacae, is an atypical etiology of bacteremia, and
is associated with malignancy, indwelling urinary catheter, and
biliary disease [12-14]. While previous case reports and case
series on Enterobacter spp. and E. cloacae have presented cases
of IE and one instance of PPM endocarditis, surveys of E. cloacae
bacteremia point to the urinary tract as the portal for bloodstream
seeding, and rarely note endocarditis as the primary source of
infection [14-17].

We present, to the best of our knowledge, the first case report of E.
cloacae AICD endocarditis. We also present a scoping study of the
existing cases and literature on E. cloacae endocarditis to highlight
important patient characteristics, clinical findings, and outcomes,
and provide a review of antibiotic recommendations for E. cloacae
endocarditis and guidelines on device removal and exchange in
CIED endocarditis.

Case Presentation
A 57 year-old male with past medical history of heart failure
with reduced ejection fraction secondary to non-ischemic
cardiomyopathy w/ AICD was directly admitted to the inpatient
cardiology service after being called in for positive blood cultures
growing E. Cloacae drawn in the emergency department 4 days
prior to admission. The patient had initially presented with
complaints of fever, malaise, shortness of breath, was tachycardic
but hemodynamically stable and without leukocytosis, and was
discharged home after blood cultures were drawn.

On admission, the patient was afebrile and hemodynamically stable,
and was initially started on zosyn (piperacillin-tazobactam) for
suspected endocarditis. Blood work was significant for leukocytosis
(12.79K/µL), and elevated C-reactive protein (CRP, 45.8 mg/L),
erthrocyte sedimentation rate (ESR, 68 mm/hr), and procalcitonin
(.77 ng/mL). He underwent transthoracic echocardiography (TTE)
on the day of admission, which revealed ejection fraction of 10%
but no vegetations or evidence of endocarditis. Infectious disease
was consulted, and recommended transitioning to cefepime and
urgent removal and replacement of the AICD. On hospital day 3,
the patient underwent tranesophageal echocardiography (TEE)
which revealed right atrial (RA) dilation, several small mobile
masses in the RA cavity associated with the device wire consistent
with small vegetations, and a larger “matted-appearing” region
associated with the device wire consistent with vegetation (Image 1).

On hospital day 9, the patient underwent unsuccessful
percutaneous AICD lead extraction, with remaining leads showing
evidence of infection requiring complete removal. The patient was
tachycardic and hypotensive post procedure, and was transferred
to the coronary care unit where he was started on milrinone and
norepinephrine for cardiogenic shock. Cardiothoracic surgery was
consulted for open chest surgery for lead removal. By hospital
day 14, the patient was successfully titrated off vasopressor and
inotropic support. On hospital day 15, the patient underwent
sternotomy with lead extraction and device reimplantation, and
he was transferred postoperatively to the cardiothoracic intensive
care unit on ventilator and vasopressor support.

On postoperative day 1 (hospital day 16), the patient was
extubated, and was titrated off of vasopressor and inotropic
support by postoperative day 5 (hospital day 20). He remained in
the cardiothoracic intensive care unit where he had peripherally
inserted central catheter (PICC) placement for continued antibiotic
course and participated in physical therapy regimen. On hospital
day 30 (postoperative day 15), the patient became hypotensive
and was started on dobutamine for cardiogenic shock. A few hours
later, the patient became unresponsiveness and pulseless, and
 cardiopulmonary resuscitation was initiated. The sternotomy was
opened at bedside and manual cardiac massage was performed with
direct intramyocardial and aortic root injection of epinephrine.
Return of spontaneous circulation was achieved, and the patient
was transferred emergently to the operation room for surgical
wash out, and placement of Swan-Ganz catheter and temporary
chest closure. Upon arrival in the operating room, the patient
hemodynamically decompensated, manual cardiac massage was
restarted, direct intramyocardial and aortic root epinephrine was
injected, and bipolar epicardial pacing leads were also placed.
Resuscitation efforts were unsuccessful and the patient expired.

Scoping Study
Materials and Methods
On December 31, 2018, a systematic search for a scoping study was
conducted using Pubmed using keywords “infective endocarditis,
Enterobacter, *Enterobacter cloacae*, cardiac device endocarditis” to identify individual case reports and cases series of *Enterobacter spp.* and *E. Cloacae* endocarditis. Case reports were reviewed individually, and when the full text in hard print copies in journal stacks, clinical data and information was interpreted from case series referencing the specific case report. All case reports and case series were reviewed and analyzed for demographic data including age and gender, past medical history, echocardiographic (either transthoracic or transesophageal echocardiography) findings, sites of septic embolism, antibiotic and surgical management, whether *E. Cloacae* was only species isolated or if there was evidence of polymicrobial infection and bacteremia, and clinical outcomes (survival or death).

**Inclusion and Exclusion Criteria**

Inclusion criteria were as follows: (1) individual case reports, case series, or case reports with accompanying reviews. (2) The patients in the cases were adults older than 18 years of age. (3) Study results could be either quantitative representation of the rates or frequency of specified clinical characteristics, or a qualitative representation of specified clinical characteristics. Exclusion criteria were as follows: (1) non-English language articles or English language articles without an available full text version; (2) articles that contained data that significantly overlapped with that of another published report.

**Results**

Systematic search revealed 13 cases of *E. cloacae* endocarditis meeting inclusion criteria [18-30], resulting in 14 total cases (including the present case) for scoping study (Table 1). The mean age was 50.2 years old with a standard deviation of 15.7. 28.6% of patients had underlying rheumatic heart disease or valvular disease, with or without previous replacement. 35.8% of patients had immunocompromising conditions such as diabetes mellitus, ...
endocarditis, and between electrophysiologists, interventional cardiologists, and vegetation presence, size, character, and potential embolic risk, of infected CIED, after completion of TEE for evaluation of endorsed by the Heart Rhythm Society recommend that in cases endocarditis [32,33]. Current guidelines and recommendations hospital mortality rates considerably higher than in HACEK endocarditis, the mortality rate remains very high, with in-rates of cardiac surgery in cases of non-HACEK Gram-negative species and fluoroquinolone considered reasonable [2]. Despite the high course of antibiotics, with antibiotic regimens including six weeks surgery is considered reasonable in combination with prolonged management as a reasonable plan of care alongside a surgical intervention. As seen in our patients, the risk factors for larger vegetations in CIED endocarditis include low ejection fraction and AICD, with vegetations developing more rapidly in patients with aforementioned risk [35]. Mortality in CIED endocarditis is high, but overall extraction-related rates are less than 1%, with extraction complications more frequently associated with open-heart surgical device removal [36]. In summary, we present the first case report of E. Cloacaecardiogenic shock, both after unsuccessful percutaneous lead extraction, and sternotomy with open surgical lead extraction and device reimplantation, in the context of extensive large vegetations demonstrate the difficulty and possible cardiovascular compromise that can result from surgical intervention. As seen in our patients, the highly uncommon nature of E. Cloacea endocarditis is rare, and the difficulty and possible cardiovascular compromise that can result from surgical intervention. As seen in our patients, the highly uncommon nature of E. Cloacea IE, Enterobacter spp, IE, and IE caused by other Gram-negative bacilli (non-HACEK) has led current guidelines on management to consider surgical management as a reasonable plan of care alongside a prolonged course of antibiotics. According to the guidelines endorsed by the Infectious Disease Society of America, cardiac surgery is considered reasonable in combination with prolonged course of antibiotics, with antibiotic regimens including six weeks of combination beta-lactams with either an aminoglycoside or fluoroquinolone considered reasonable [2]. Despite the high rates of cardiac surgery in cases of non-HACEK Gram-negative endocarditis, the mortality rate remains very high, with in-hospital mortality rates considerably higher than in HACEK endocarditis [32,33]. Current guidelines and recommendations endorsed by the Heart Rhythm Society recommend that in cases of infected CIED, after completion of TEE for evaluation of vegetation presence, size, character, and potential embolic risk, lead extraction is recommended with appropriate consultations between electrophysiologists, interventional cardiologists, and cardiac surgeons for surgical planning [34]. CIED reimplantation is recommended after blood cultures are negative for at least 72 hours or longer depending on the specified clinical picture for [34].

Our patient’s hemodynamic decompensations and progression to
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