Open Journal of
Clinical & Medical
Case Reports

Volume 2 (2016)
Issue 18

ISSN 2379-1039

A Case of *Escherichia Coli (E. Coli)* Infective Endocarditis

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Abstract

Although rarely reported, *Escherichia coli* bacteremia has the potential to become a causative agent of infective endocarditis (IE). Of these reports, very few of them document native cardiac valve involvement and this may be partially explained due to the overall structure and origin of *E.coli*. In this case, we describe a patient with an extensive renal history that developed a large mitral valve vegetation, as well as severe thrombocytopenia, septic emboli, and multiple cerebral infarcts. We also compare common risk factors for this type of atypical IE and discuss the management strategy to decrease overall morbidity and mortality.

Keywords

Escherichia coli (E. coli); infective endocarditis (IE); bacteremia; gram-negative bacilli; urinary tract infection (UTI)

Abbreviations

Escherichia coli (E. coli); IE: infective endocarditis; yo: year old; RLQ: right lower quadrant; SLE: Systemic Lupus Erythematosus; UTI: urinary tract infection; ED: emergency department; bpm: beats per minute; BP: blood pressure; RUQ: right upper quadrant; PMN: polymorphonuclear leukocytes; Hgb: haemoglobin; GFR: glomerular filtration rate; BUN: blood urea nitrogen; CR: creatinine; LDH: lactate dehydrogenase; ESR: erythrocyte sedimentation rate; PTT: partial thromboplastin time; PT: prothrombin time; INR: international normalized ratio; ICU: intensive care unit; TTP: thrombotic thrombocytopenic purpura; HUS: hemolytic uremic syndrome; IV: intravenous; ANA: antinuclear antibodies; CT: computed tomography; MRI: magnetic resonance imaging; TEE: transesophageal echocardiogram; cm: centimetre; CBC: complete blood count; CVA: cerebrovascular accident; g: gram; ICE-PCS: Infective Endocarditis Prospective Cohort Study; GU: genitourinary; CRP: C-reactive protein

Introduction

The following is a case presentation of a patient who developed a rare form of endocarditis caused by the bacteria *Escherichia coli.* This article describes the patient's clinical presentation, discusses reasoning behind why such events may have occurred, and considers a general approach to future patients with similar clinical manifestations.

Case Presentation

A 30 year old Caucasian female presented to the emergency department complaining of malaise and one episode of hematemesis. The patient's fiancé reported coming home from work to find the patient resting on the couch with dark, dried blood around the inside of her mouth. She had been

progressively less active in the preceding week with complaints of recurrent headaches, fatigue, and painful swelling in her lower extremities. She admitted to losing nearly 30 pounds within this time and attributed the weight loss to having decreased appetite, nausea, and intermittent right-sided lower back pain that radiated to the RLQ of her abdomen. She described the pain as aching in quality and moderate in severity, with episodes lasting several minutes in duration. She denied any dizziness, loss of consciousness, shortness of breath, diarrhea, constipation, dysuria, recent illness or sick contacts.

The patient had a past medical history of multiple urinary tract infections, pyelonephritis, left kidney hydronephrosis, and recurrent renal calculi, all occurring within the previous three years. For treatment of her recurrent renal calculi, she had received lithotripsy therapy and implantation of a left double j ureteral stent. Previous records indicated the ureteral stent was placed three years prior to admission and scheduled to be removed 6 months post-implantation, but was not completed due to lack of patient follow-up. Other past surgical history included unilateral tubal ligation. Her OB/GYN history was that of *gravida* 3 and *para* 1021 with irregular menses and amenorrhea for 2 months. There was a family history of SLE with her sister. She had allergies to aspirin, gentamicin, iodine, and NSAIDs. She consumed alcohol socially, was an eleven pack-year smoker, and denied drug use.

In the ED, the patient was in no acute distress. She appeared malnourished, pale, and weak. Vital signs revealed tachycardia 108 bpm, tachypnea 22 breaths/min, hypotension 88/69 BP, and fever with a temperature of 101.3*F. The patient presented with pale conjunctiva, poor dentition, crusted blood covering the gingiva, and dry mucosal membranes. Cardiac exam was within normal limits and without any extra heart sounds. Lungs were clear to auscultation bilaterally with good air entry. Abdomen was mildly distended with diffuse abdominal wall petechiae, normal bowel sounds, and no signs of hepatosplenomegaly. Patient experienced severe pain in the RUQ, RLQ, and epigastric region upon light palpation. Costovertebral angle tenderness was present on the right side. Bilateral pitting edema was present to the distal third of the lower legs. Linear excoriations and moderate petechiae covered the anterior right lower leg. All other physical exam findings were within normal limits.

Initial labs drawn from the ED revealed leukocytosis (28,900/mm3) with bandemia (65% PMN; 28% bands), anemia (Hgb 8.9 g/dL), severe thrombocytopenia (9,000/mm3), renal failure (GFR 7, BUN 106, CR 7.04), and an elevated serum LDH (566). ESR, PTT, PT, and INR were within normal reference range. Serum sodium, potassium, chloride, and calcium levels were within normal reference range. The patient was admitted to the ICU for suspicion of sepsis and TTP-HUS. She was empirically treated with IV metronidazole, piperacillin/tazobactam, and high-dose corticosteroids.

In the ICU, the patient received emergent hemodialysis for treatment of uremia. She received 2 units of platelets once hematology reported the peripheral blood smear lacked schistocytes and other evidence consistent with TTP. They believed the source of thrombocytopenia was secondary to sepsis. An ultrasound of the kidneys, ureters, and bladder revealed moderate right-sided hydronephrosis with a dilated proximal ureter. Also, there were non-obstructing renal calculi located in the right and left renal pelvis. Repeat CT of the abdomen and pelvis was recommended, which revealed multiple bilateral renal calculi with right ureteral obstruction, mild right-sided hydronephrosis, a left double j ureteral stent with significant encrustation, a left atrophic kidney, and a hyper dense calcified bladder (Figure 1).

A Foley catheter was inserted and drained a minimal amount of dark-brown, cloudy urine.

Infectious disease was consulted and recommended switching antibiotic coverage to IV metronidazole and cefepime while blood and urine cultures were pending. Concern for an autoimmune disorder was advocated as a possible etiology for the severe thrombocytopenia. Therefore, rheumatoid factor, immunoglobulin G, and antinuclear antibody (ANA) levels were ordered.

The next morning, the patient's mental status significantly deteriorated and platelet levels again measured to be 9,000/mm3. The patient was unable to communicate verbally and would not respond to simple commands (e.g. moving her leg). She presented with a left-sided flexural position of both upper and lower extremities. Left ankle rigidity was also noted. A head CT was ordered for concern of a possible stroke and due to inadequate findings, a non-contrast MRI of the brain was recommended. Results of the MRI revealed an acute finding of multiple brain infarcts located in bilateral thalamic areas, the cerebellar lobes, left occiput cortical tissue, and bilateral cerebral hemispheres. These findings were concerning for an embolic event. Subsequently, transesophageal echocardiogram (TEE) was ordered and revealed a large (1.9 x 1.2cm) mobile vegetation attached to the anterior leaflet of the mitral valve. At this time, preliminary results of blood and urine cultures revealed growth of gram-negative bacilli with identification to follow. Given a positive family history for SLE, additional investigation for Lupus anticoagulant, anti-DNase B-titer, and anti-DNA was warranted. The patient was transferred to a nearby hospital that was more equipped for further care.

Following transfer, the patient was treated empirically with ceftriaxone and levofloxacin. Identification of blood and urine cultures eventually revealed growth of *E.coli* susceptible to all tested antibiotics. The patient remained on the previously noted antibiotics and was also started on micafungin (later switched to fluconazole following sensitivity results) when repeat blood cultures grew *Candida albicans* without resistance. Her health was further complicated after she developed status epilepticus, confirmed by EEG and alleviated with lorazepam and forphenytoin. Phenytoin was added afterwards for maintenance therapy. The patient's thrombocytopenia was improved (>50,000/mm3) after receiving 3 units of platelets and 1 unit of cryoprecipitate. Serology results were relayed by the admitting hospital and included the following: mildly elevated rheumatoid factor (transfer hospital repeat labs were within normal reference range); mildly elevated homogenous and speckled ANA; immunoglobulin G was within normal reference range; real-time PCR assay for Hepatitis B and C infections were not detected; and HIV antibody screening was negative. Given the atypical nature of the patient's disease, multiple organ involvement, and overall deterioration, the patient was given high-dose corticosteroids for concern of hemophagocytic lymphohistiocytosis. However, a repeat TEE confirmed the presence of a mitral valve vegetation, but the patient was not a surgical candidate due to presence of a large cerebrovascular accident (CVA) at the time of transfer. Therefore, the dose of ceftriaxone was increased from 1g to 2g for efficient cardiac penetration.

After nephrology and urology were consulted, the patient received a second hemodialysis treatment. As a result, her renal function and overall mental status greatly improved. Urology was able to surgically address a right complex cystand obstructing renal calculus via ureteral stent placement (subsequently removed 5 days later after urine output improved). They also performed multiple cystolithotomy and pyelolithotomy procedures, which resulted in good post-op urine output.

One week following the transfer, similar sized mitral valve vegetations were again confirmed by

TEE after the development of a Mobitz type II with 2:1 heart block, intermittent in nature. At this time, the patient declined further treatment and signed herself out against medical advice. She was provided discharge instructions for re-evaluation by follow up TEE within two weeks.

Discussion

We report here a rare case of infective endocarditis caused by *E. coli*, which satisfied one major (cardiac valve leaflet vegetation present on echocardiography) and three minor (fever, major arterial emboli, and elevated rheumatoid factor) in modified Duke's criteria for the clinical diagnosis of IE [1]. In a cohort study compiled by the ICE-PCS (Infective Endocarditis Prospective Cohort Study) database, among the 2761 patients found to have endocarditis, less than 1% of them were due to *E.coli* [2]. *Micol et al.* further reported that only 36 cases of IE have had Duke criteria definite *E.coli* native valve endocarditis between 1909 and 2002 [3].

The scarcity of *E.coli* induced IE may be first explained by the location and nature of the bacteria itself. In vitro studies have shown that gram-negative bacilli, such as *E.coli*, have less of a capability for adherence to native cardiac valve leaflets than that of coagulase-positive and coagulase-negative staphylococci, streptococci, and enterococci [4]. These findings can be partially explained by reviewing the type of adhesion molecule associated with most *E.coli* infections involving the genitourinary (GU) tract. The bacteria typically express type 1 fimbrial FimH adhesion molecules that adhere to the mannose-specific integrins found on urothelial cells [5]. However, these integrins were not found to be located on the endothelial cells of native cardiac valves [6]. Given the significant history of pyelonephritis and obstruction in our patient, there is little doubt that the *E.coli* portal of entry was the GU tract with subsequent bacteremia and dissemination. Although pathological confirmation would have been ideal for confirming IE and ruling out Libman-Sacks complicated by *E.coli* bacteremia, we relied on modified Duke's criteria for our diagnosis. Consideration for an alternative diagnosis secondary to abnormal lab values was addressed. The initially elevated rheumatoid factor, although commonly used, lacks sensitivity and specificity due to high rates of false positive results [7]. Also, inflammatory markers such as ESR and CRP are non-specific and typically elevated in inflammatory states. Either ESR or CRP may be normal despite infection or inflammation [8].

In an 18-year prospective survey of 3605 bacteremia episodes, *E.coli* accounted for nearly 25% of the cases and the most common focus was that of the urinary tract. Nevertheless, only 2 of those patients developed IE [9], which lead us to further research for similarities among cases. The most comparable case to our knowledge was a 54yo Indian male with a past medical history of diabetes mellitus and hypertension who developed *E.coli* urosepsis, native valve endocarditis, and an acute transient ischemic attack following ureteric stent implantation due to hydroureternephrosis [10]. The overriding similarities between our cases are as followed: the urinary tract was the origin of insult; both required ureteral stent implants and had chronic inflammatory conditions (diabetes in the preceding case, recurrent obstructive nephrolithiasis in our case); *E.coli* hematogenously disseminated, adhered, and produced vegetations along native cardiac valve leaflets; and both patients suffered an ischemic stroke. Although two recent reviews describe certain risk factors for *E.coli* endocarditis to be advanced age, female gender, diabetes, prosthetic valve, and preceding UTI [3,11], we would also like to further expand this list by adding the following risk factor: chronic inflammatory conditions involving the GU tract

(e.g. obstructed kidneys, grossly infected GU stents). By doing so, this could raise suspicion for atypical IE in those patients with a positive blood culture for *E.coli* and an extensive urinary tract medical history.

Conclusion

In conclusion, our case highlights a severe complication that can be seen with *E.coli* bacteremia, especially in the setting of a chronic systemic inflammatory state induced by a grossly infected GU tract. We relied on modified Duke's criteria for our clinical diagnosis of IE, but acknowledge the lack of pathological evidence. We agree with *Branger et al.* that early echocardiography should be considered for all individuals with *E.coli* bacteremia. We also agree with multiple sources that early valve replacement is likely to decrease overall mortality rates and wish to add likely to decrease overall morbidity as well [11,12,13]. Early screening and surgical intervention may have prevented a few of our patient's complications, such as the embolic events that our patient experienced. It may also prevent future patients from surgical contraindications, such as severe thrombocytopenia and cerebrovascular accidents. Lastly, we believe that antibiotic therapy should be escalated to a therapeutic level for cardiac penetration if there is high clinical suspicion or evidence of IE, or in cases of persistent bacteremia.

Acknowledgement

We would like to thank St. Anthony's Hospital and staff for their hard work and dedication to helping our patient during her illness.

Figure

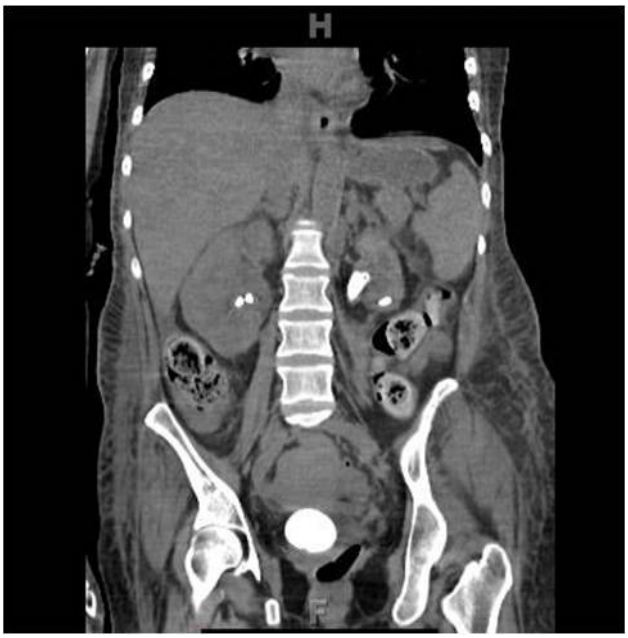

Figure 1: CT-scan of the abdomen and pelvis. Cross sectional view showing hyper dense regions involving the bladder, as well as the right and left renal pelvis. Renal calculi in bilateral kidneys and right-sided hydronephrosis may also be seen.

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Manuscript Information: Received: June 25, 2016; Accepted: September 20, 2016; Published: September 22, 2016

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Citation: Knight R, Pulvirenti J, Mena Lora AJ. A case of *Escherichia coli (E. coli*) infective endocarditis. Open J Clin Med Case Rep. 2016; 1164

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