

Late Prosthetic Valve Endocarditis Caused By *Burkholderia cepacia* And *Candida dubliniensis*-The First Reported Case In The Medical Literature

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Citation

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Abstract

Background:

Prosthetic valve endocarditis (PVE), a life threatening condition, may arise early or late after cardiac valve surgery. It poses a high morbidity and mortality threat if not promptly diagnosed and treated.

Case presentation:

We report an interesting case of a 47-year-old male with recurrent endocarditis who presented with a one day history of progressive shortness of breath and increasing bilateral lower extremity edema. Transthoracic echocardiography (TTE) showed decreased left ventricle function with regional wall motion abnormalities, tricuspid regurgitation, and vegetations on the aortic valve. Blood cultures grew *Burkholderia cepacia* (*B. cepacia*) a sensitive to cefepime and *C. dubliniensis* sensitive to caspofungin. The patient was successfully treated with IV caspofungin and IV cefepime for 6 weeks and discharged from the hospital to a skilled nursing facility (SNF) and then to a rehabilitation center. Although, cases of early PVE with *B. cepacia* have been reported previously, but to the best of our knowledge, this is the first reported case of late PVE with *B. cepacia* and *C. dubliniensis* in the medical literature. The subject of this article is to present our experience with this exceedingly rare case of late PVE.

Conclusion:

PVE is very rarely caused by *B. cepacia* and *C. dubliniensis*. Prompt management of PVE by appropriate therapy can significantly reduce the morbidity and mortality risk associated with PVE.

INTRODUCTION

Valvular heart disease is very complex with potentially fatal consequences (1). It can be managed either medically or surgically. Cardiac valve replacement with mechanical valves or bioprosthetic valves has been an effective therapeutic modality in the management of valvular heart disease. Cardiac valve replacement is not without complications. Some of the complications associated with mechanical valves are thromboembolic requiring long-term anticoagulation; however, mechanical valves are structurally strong with low incidence of configuration failure. While complications of prosthetic valve include: structural deterioration, valve obstruction due to pannus formation, & paravalvular leak. The occurrence of these complications depends on the type of valve used, the position of the valve, structural or underlying heart disease, age and sex of the patient (7-9), and other co-morbid factors. The incidence of

complications in patients undergoing cardiac valve surgery is about 3% annually (2-6). Infection is often a major feared complication post cardiac valve surgery. It can arise early or later after surgery.

Prosthetic valve endocarditis (PVE) is classified as either early PVE or late PVE. Early PVE is acquired perioperatively and late being unrelated to the valve operation. There is decreased incidence of early PVE due to antibiotic prophylaxis. Late PVE is more severe, causing death in 15% of the patients. The epidemiology, pathogenesis, microbiology and clinical manifestations of both early and late PVE are different. Studies have shown that the risk of acquiring PVE is highest during the first three months after cardiac surgery and then it gradually falls to a rate of 0.4% annually. (10-14). The predictability of pathogens causing PVE becomes apparent when categorizing PVE by time after implantation. (1, 15). The usual pathogens causing

early PVE (within two months of implantation) in decreasing order of frequency include: *S. aureus*, coagulase negative staphylococci, culture negative and very rarely *B. cepacia* and *C. dubliniensis*; Similarly, late PVE (after two months of implantation) is usually caused by coagulase negative staphylococci, staphylococci, culture negative, enterococci, and viridans streptococci. Although, reports of early PVE caused by *B. cepacia* and *C. dubliniensis* have been reported previously, however, to the best of our knowledge, there have not been any reports of *B. cepacia* and *C. dubliniensis* causing late PVE. Graphs (11)

B. Cepacia (formerly *Pseudomonas cepacia*), an aerobic, catalase positive, glucose non fermenting gram negative rod was first described in 1949 by Walter Burkholder as the agent responsible for onion skin rot and as a opportunistic pathogen in the mid 1950s (16) it is known for its resilient nature and can survive inhospitable environments with minimal nutrients. (17) studies show that it can well survive a 10% iodine solution for over a year and to be the culprit causing pneumonia in patients with underlying lung disease such as cystic fibrosis, leading to complications and increasing the morbidity and mortality rate in such patients (18-19).

C. dubliniensis, a fungal opportunistic pathogen was first isolated in 1995 from patients with human immunodeficiency virus (HIV) (20) studies have shown that it can cause both mucocutaneous as well as invasive disease leading to fungemia, especially in patients with a weak immune system such as patients receiving bone marrow, solid organs or those infected with HIV. It has often been a diagnostic challenge to laboratory personnel to distinguish *C. dub* from *C. albicans* with routine lab methods; therefore, molecular techniques such as real-time multiplex PCR are recommended in the identification of *C. dub*. (21-24) The management of PVE depends on the type of bacteria or fungi isolated from the blood cultures and their sensitivities to the antibiotics and antifungals.

In this article, we present the first reported case of late PVE caused by *Bulkholderia cepacia* and *Candida dubliniensis*.

CASE REPORT

A 47-year-old white male presented to the emergency room (ER) complaining of progressive and severe shortness of breath, increasing bilateral lower extremity edema and a twenty six pound weight gain over a two month period. He also complained of paroxysmal nocturnal dyspnea,

orthopnea, occasional nausea and vomiting, productive cough in the morning, and discomfort from his tense edema in the lower extremities bilaterally. The patient denied fever, chills, diarrhea, constipation, and chest pain.

His past medical history was significant for IV drug abuse with heroin, hepatitis C, recurrent endocarditis status post aortic and mitral valve replacements, coronary artery disease status post myocardial infarction, congestive heart failure, right heart failure, atrial fibrillation, seizure disorder, antisocial personality disorder, polysubstance abuse, and chronic stasis dermatitis. The patient was hospitalized and treated for bacterial and fungal endocarditis with caspofungin and cefepime two months ago/prior to this event. His past surgical history included surgery for an incarcerated umbilical hernia, a cervical spine fracture, open reduction internal fixation of right tibia-fibula fracture, and two vessel coronary artery bypass graft (CABG). Additionally, the patient had tissue aortic valve and mitral valve replacement with subsequent mechanical mitral valve replacement a year later about ten years prior to his admission to our ED.

On physical examination, the patient was found to be in severe distress and afebrile. Upon cardiac examination, a loud click was heard and the heart rate was irregularly irregular. Significant bilateral lower extremity edema with chronic stasis dermatitis bilaterally was also noted. Electrocardiography showed atrial fibrillation with a left bundle branch block. Chest x-ray showed cardiomegaly and signs of congestive heart failure. Transthoracic echocardiography (TTE) revealed decreased left ventricle function with regional wall motion abnormalities, mild aortic insufficiency, bi-atrial enlargement, severe tricuspid regurgitation with pulmonary hypertension, and vegetation on the aortic valve.

Laboratory tests revealed: serum sodium 133 (reference range [RR] 140-150); aspartate aminotransferase 56 (RR <38); alkaline phosphatase 204 (RR 40-129). Urinalysis was unremarkable but urine toxicology screen was positive for opiates.

Blood cultures grew *B. cepacia* sensitive to cefepime and *C. dubliniensis* sensitive to caspofungin. The patient was successfully treated with IV caspofungin and IV cefepime for 6 weeks. The patient was successfully treated with and discharged from the hospital to a rehabilitation center.

Figures A and B showing vegetations on the aortic valve

Figure 1

Figures A

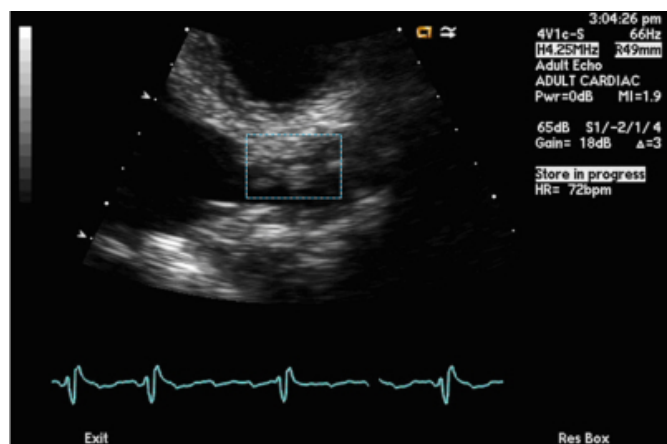
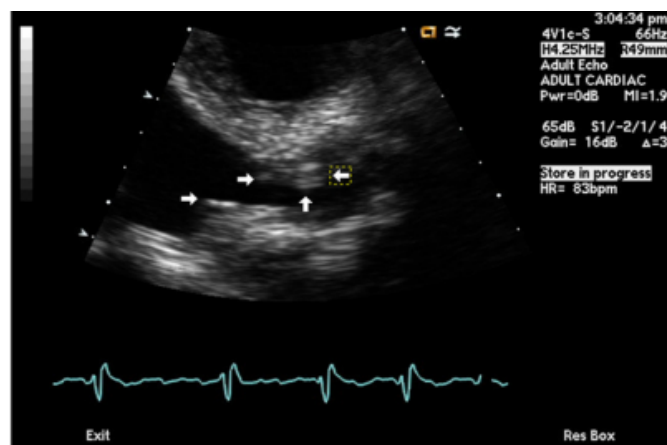


Figure 2

Figure B



DISCUSSION

A common complication following replacement of a diseased heart valve with a prosthetic valve is endocarditis. The presenting signs and symptoms are similar to those occurring in native endocarditis and include: fever, heart murmur, and septic emboli. The diagnostic modalities include: Transesophageal echocardiography (TEE) and transthoracic echocardiography (TTE). Although, TTE has a low sensitivity but its specificity approaches 100% (25) Contrary, TEE has a much higher sensitivity rate than TTE and is much more sensitive than TTE in detecting vegetations and abscess, and in the diagnosis of PVE.

LPVE is a diverse disorder with many different prognostic scales. It is important to distinguish the most severe prognosis from the least severe as early as possible. The two treatment modalities include medical and surgical approaches. Surgical treatment carries better prognosis in

LPVE with specific features. Karchmer et al. (26) provided criteria for choosing one therapy over the other. They suggest an early surgical intervention for patients with LPVE who have at least two of the following: nonstretococcal etiology, undue persistence of fever despite antibiotic therapy, a new regurgitant murmur, and congestive heart failure associated with prosthesis dysfunction.

LPVE is a severe condition carrying a high mortality and morbidity rate. Thus, it is important to prevent any incidence of LPVE development using prophylactic antibiotics. The American Heart Association currently recommends antibiotic prophylaxis during dental procedures in patients with prosthetic cardiac valve, history of previous endocarditis, and cardiac transplant recipients with valvular disease. It recommended prophylaxis in congenital heart disease in the following cases: Unrepaired cyanotic heart disease, repaired congenital heart disease with prosthetic material, and repaired congenital disease with residual defect at the site of prosthetic device. In our patient, TEE revealed decreased left ventricle function with regional wall motion abnormalities, mild aortic insufficiency, bi-atrial enlargement, severe tricuspid regurgitation, and vegetations on the aortic valve. Upon suspecting endocarditis, blood cultures were obtained prior to broad spectrum antibiotic therapy. Two sets of aerobic and anaerobic broth media were used for blood sample inoculation. Bacteria or fungi isolated from the positive blood cultures were then tested for antibiotic susceptibility in the microbiology laboratory by using the standard disc diffusion method. The treatment plan was determined based on the antibiotic susceptibility test results. Our patient was successfully treated with IV caspofungin and cefepime for 6 weeks.

Tables 1 and 2 illustrate susceptibility results for both *B.cepacia* and *C.dubliensis* isolated from the patients blood culture.

Figure 3

Table 1-B. cepacia

Ampicillin	Resistant
Ampicillin/Sulbactam	Resistant
Cefazolin	Resistant
Cefepime	Sensitive
Cefuroxime	Sensitive
Ciprofloxacin	Sensitive
Gentamicin	Sensitive
Imipenem	Sensitive
Piperacillin/Tazobactam	Sensitive
Trimethoprim/Sulfa	Sensitive

Figure 4

Table 2-C.dubliensis

Fluconezol	Sensitive
Caspofungin	Sensitive
Voriconazole	Sensitive
Amphotericin B	Sensitive

CONCLUSION

Prosthetic valve endocarditis is a major post-operation complication. It may arise early or late after the surgery. Early infection is usually caused by direct contamination during surgery or through hematogenous spread during the early phase (27). In the early phase, the, endothelialization has not occurred yet, thus the structure is still coated with host proteins, making it prone to organism adherence (27). However, in the late phase, endothelialization alters the site of adherence making the pathogenesis of late prosthetic valve similar to the native valve endocarditis (27). The best test for diagnosis is TTE which shows early vegetations that cannot be visualized by TEE (28).

Endocarditis prophylaxis is extremely important in patients with prosthetic heart valves undergoing invasive procedures. In a study by Horstkotte, in 533 patients with prosthetic heart valves, antibiotics were given to 304 patients before going for invasive procedures, while 229 similar patients did not receive any prophylaxis antibiotics (29). As a result, none of the patients on prophylaxis developed endocarditis, while 6 patients on no antibiotic therapy developed endocarditis.

Bacteremia and/or fungemia, occurring early or late after cardiac valve surgery, has been associated with fatal consequences if not appropriately managed. Therefore, prompt management of both early and late PVE medically

by appropriate antibiotics and antifungals and surgically by valve replacement treatment can significantly reduce the morbidity and mortality caused by these pathogens.

Although, there have been reports of PVE caused by *B. cepacia* and *C. dubliniensis* early after surgery, but to the best of our knowledge this report represents the first published case of PVE by these pathogens late after surgery.

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