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Case Report

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Corynebacterium diphtheriae Native Aortic Valve Endocarditis in a Patient With Prosthetic Mitral Valve: A Rare Presentation

Orathai Pachirat[a, c], Danon Kaewkes[a], Burabha Pussadhamma[a], George Watt[b]

Abstract

Infective endocarditis due to non-toxigenic *Corynebacterium diphtheriae* is uncommon. We describe the case of a 42-year-old male with a history of mitral valve replacement with prosthetic valve for 4 years. He presented with fever, weight loss, dyspnea on exertion and orthopnea. The echocardiography demonstrated large vegetation attached on the left coronary cusp of the aortic valve with moderately severe aortic regurgitation but sparing of the prosthetic mitral valve. Three separate blood cultures grew *Corynebacterium* species. The patient underwent aortic valve replacement due to valvular dysfunction and congestive heart failure. *C. diphtheriae* DNA was detected by 16 S rDNA polymerase chain reaction (PCR) from the heart valve tissue. The patient recovered completely with combine antibiotics and surgical intervention. He was discharged from the hospital with good clinical outcome.

Keywords: *Corynebacterium diphtheriae* endocarditis; PCR; Bloodstream infection; Aortic valve endocarditis

Introduction

Corynebacterium diphtheriae (*C. diphtheriae*) was first isolated by Loeffler in 1884 as the causative agent of diphtheria, a disease in which infection is localized to the respiratory tract due to diphtheria toxin [1, 2]. Infective endocarditis (IE) due to non-toxigenic *C. diphtheriae* is an uncommon. However there have been increasing numbers of the reports of IE being caused by this organism [3-7]. Most patients with *C. diphtheriae* endocarditis have underlying cardiac diseases especially prosthetic heart valves, a history of intravenous drug use, a history of alcoholism, homelessness or hepatic cirrhosis [8-11]. Recommendations for treatment based on expert opinion suggest that 4 - 6 weeks of a β-lactam antibiotic in conjunction with an aminoglycoside be given [12]. Here we described a patient with a mitral prosthetic heart valve who developed infective endocarditis on the native aortic valve due to *C. diphtheriae* but sparing of prosthetic mitral valve.

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[a]Division of Cardiology, Department of Medicine, Khon Kaen University, Khon Kaen, Thailand
[b]International Emerging Infections Program (IEIP), Thailand MOPH-US CDC, Collabolation, Nontaburi, Thailand
[c]Corresponding Author: Orathai Pachirat, Cardiovascular Unit, Department of Medicine, Khon Kaen University, 123 Mitraparp Highway, KhonKaen, 40002, Thailand. Email: rathai@hotmail.com

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Case Report

Patient information

A 42-year-old male, poultry farmer with underlying rheumatic heart disease, severe mitral stenosis and mild aortic regurgitation was performed mitral valve replacement with 23-mm St. Jude in 2007. He presented to a local hospital with a 4-week history of fever and associated weight loss, night sweat, shortness of breath and dyspnea on exertion. He denied any history of intravenous drug use, smoking, or alcohol consumption. He was found to be in high fever and was transferred to our cardiac center for evaluation.

Clinical findings

On admission, he had fever of 40 °C, blood pressure was 124/68 mm Hg, heart rate was 110 beats/min with irregular rhythm (Fig. 1), and respiratory rate of 21/min. There was no cyanosis, mild pale and mild jaundice, without distension of the jugular vein. Cardiovascular examination revealed diastolic blowing murmur grade 3/6 at LLSB with an audible valve click with both basal pulmonary crackles, abdomen showed mild hepatomegaly, no splenomegaly and no ankle edema of both extremities. Further systemic examination showed no evidence of peripheral stigmata of endocarditis or liver cirrhosis.

Diagnostic focus

Laboratory data (Table 1) revealed white blood cell count of 8,800/μL with 86% neutrophils and normal platelets count. Blood urea nitrogen level was at 12.4 mg/dL, and creatinine level was at 1.0 mg/dL. Chest X-ray showed cardiomegaly with

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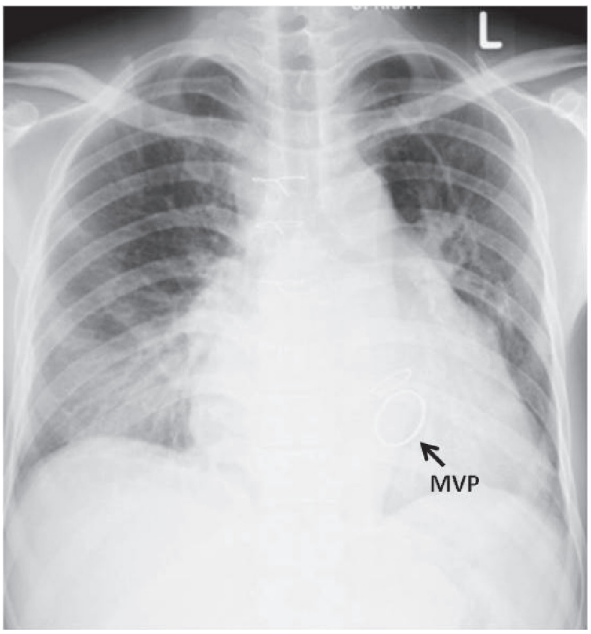

Figure 1. Chest X-ray showing cardiomegaly with pulmonary congestion and mitral valve prosthesis (MVP).

pulmonary congestion (Fig. 2). Three sets of aerobic blood culture that were taken from different venipuncture sites with the first and second separate by at least 1 h at admission before any antibiotic therapy grew *Corynebacterium spp*. Possible endocarditis was diagnosed and intravenous ceftriaxone 2 g with amikacin 15 mg/kg/day in divided dose were administered.

The transthoracic echocardiogram (TTE) was performed on the first day of admission, which revealed a large mobile vegetation measuring 0.9 × 1.3 cm on the ventricular aspect of left coronary cusp of the aortic valve, which destroyed the aortic valve cusp, causing moderately severe aortic regurgitation and minimal pericardial effusion. The transesophageal echocardiography (TEE) was performed 1 day later to examine for prosthetic valve involvement. The findings of both TTE and TEE were consistent with endocarditis of the aortic valve. Prosthetic mitral valve function was normal without evidence of endocarditis (Figs. 3, 4).

Therapeutic intervention and follow-up

The patient received intravenous antibiotics on the first day of hospitalization, and was referred to cardiothoracic surgeons for surgical intervention due to unresolved fever after 8 days of medical treatment with large highly mobile vegetation and severely destroyed aortic valve with severe aortic regurgitation.

C. diphtheriae was detected by real-time PCR in cardiac valve tissue [13, 14]. Two weeks after surgery, the patient was discharged from the hospital with good clinical outcome and regular follow-up every month.

Discussion

C. diphtheriae is a Gram-positive, aerobic, pleomorphic coccobacillus, frequently with "club- shaped" morphology. Invasive infection with non-toxigenic *C. diphtheriae* is rare. Currently, little is known about the pathogenesis and epidemiology of such infections. In Thailand, there was two published data of *C. diphtheriae* endocarditis in children [15, 16], no data in adult patients. This is the first case of adult *C. diphtheriae* endocarditis. Isolation of non-toxigenic *C. diphtheriae* has been reported with increasing frequency in publications from many other countries [17-21]. Typical nearly two-thirds of patients have underlying valvular heart disease. It is described as an aggressive and destructive disease, similar to *Staphylococcus aureus* endocarditis, with a high rate of complications and mortality. This is because *C. diphtheria*e tend to result in large vegetations, systemic embolization and mycotic aneurysms [22].

Cardiac abnormalities, including congenital cardiac abnormalities and prosthetic heart valve have been described as risk factors for *C. diphtheriae* endocarditis [17-19]. In our case, infection involved the native aortic valve but sparing of the prosthetic mitral valve. The reason for the selective native aortic valve than prosthetic mitral valve is uncertain. No other case reports have similar findings.

Endocarditis as a result of this organism causes valvular destruction and valvular dysfunction with heart failure and frequent embolic complications. In our case illustrated only large vegetation and valvular dysfunction on the native aortic valve with clinically sepsis, no sign of metastatic emboli, so we did not performed computed tomography (CT) or magnetic resonance imaging (MRI) of affected organ.

There are no recommended guidelines for treatment of IE caused by *C. diphtheriae*. Therapy of this endocarditis in literatures has varied depending on hospital practice or expert opinions. Combination of antibiotics therapy, β-lactam and aminoglycoside antibiotics are usually described for 4 - 6

Table 1. Laboratory Data

	Results
CBC	Hb: 12.8 g/dL, HCT: 34.8%, WBC: 8,800 / µL; N: 86%, L: 10%, Mono: 2%, band form: 2%, platelets: 153,000/µL
Kidney function	BUN: 12.4 mg/dL, creatinine: 1.0 mg/dL
LFT	Bilirubin (total): 4.3 µmol/L, bilirubin (direct): 3.7 µmol/L, AST: 41.0 IU/L, ALT: 18 IU/L, AP; 230 IU/L, protein: 5.6 mg/dL, albumin: 2.8 mg/dL
Electrolyte	Na: 128.0 mmol/L, K: 4.0 mmol/L, Cl: 86 mmol/L, HCO_3 29 mEq/L

CBC: complete blood count; HCT: hematocrit; WBC: white blood cell; LFT: liver function test; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

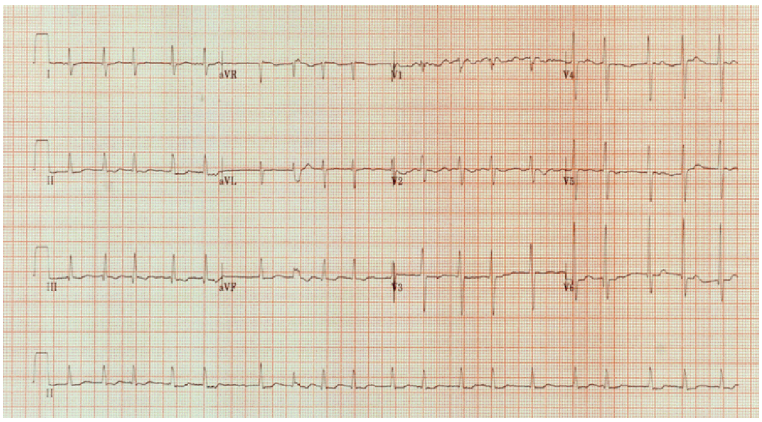

Figure 2. Electrocardiography showing atrial fibrillation with rapid ventricular response.

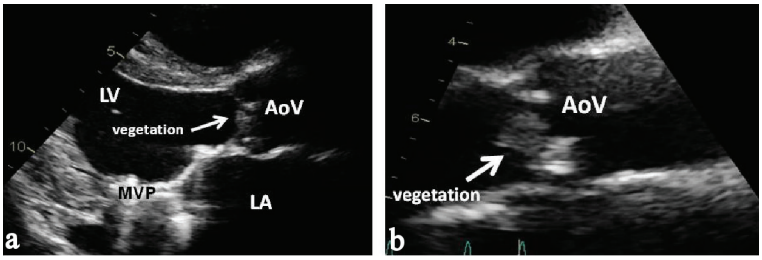

Figure 3. Transthoracic echocardiogram showing normal mitral valve prosthesis (MVP) (a), and large vegetation on the aortic valve (AoV) (b).

weeks. Our patient received intravenous ceftriaxone and amikacin for 4 weeks with early surgical intervention (aortic valve replacement) with good outcome.

Diphtheroid organisms are often regarded as contaminants when found in blood culture. In addition, because of the absence of underlying cardiac risk factors in many of these patients, the clinician must be aware of the possibility of invasive *C. diphtheria*e endocarditis, which could lead to delayed diagnosis and treatment. The diagnosis of endocarditis was made in all cases based on isolation of the organism from the blood stream, as well as the fact that clinical presentation was consistent with infective endocarditis. The aortic valve involvement in our patient is consistent with the findings of another report that *C. diphtheriae* seem to have a predilection for left sided valves [21, 22]. Interestingly, our patient had mitral prosthetic heart valve but no evidence of prosthetic valve endocarditis according to echocardiography and surgical finding. This report of *C. diphtheriae* endocarditis was confirmed by molecular detection (PCR) of bacterial genes in the heart valve tissue.

Conclusions

We described a rare clinical presentation of *C. diphtheriae* endocarditis. For the successful treatment of this IE, early diagnosis is important and the patient should be managed in a center in which a multidisciplinary team (endocarditis team) is available for immediate surgical intervention.

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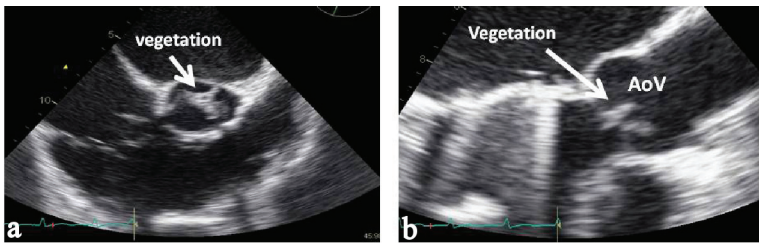

Figure 4. Transesophageal echocardiogram showing vegetation on the aortic valve (AoV) cross-sectional view (a), and long-axis view (b).

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Conflict of Interest

None of the authors has any potential conflict of interest to report.

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