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Case Report Open Access

Nontoxigenic *Corynebacterium diphtheriae*: A Rare Cause of Infective Endocarditis in Native Valve

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Abstract

We report a case of non-complicated endocarditis due to nontoxigenic *Corynebacterium diphtheriae* that occurred on a native valve. The patient had no known risk factors for endocarditis, but he had poor social circumstances. He received penicillin in conjunction with an aminoglycoside therapy. Evolution was marked by the sterilization of blood cultures but persistence of small vegetation with mild mitral regurgitation. The patient was discharged and followed in consultation twice per month during 3 months and twice year after with good clinical and biological status.

Keywords: Nontoxigenic *Corynebacterium diphtheriae*; Native valve

Introduction

Infective Endocarditis due to nontoxigenic *Corynebacterium diphtheriae* is an uncommon infection. It was first described in 1884 by Loeffler as the causative agent of diphtheria and the first case of infective endocarditis caused by this organism was reported in 1893 [1-2]. Toxin production may cause disseminated illness with pharyngeal membrane production, myocarditis and neurological and renal dysfunction [3]. The outcome can be good if patients are carefully selected for medical or surgical treatment.

Case Report

A 21-years-old male with no significant past medical history, who had received diphtheriae vaccine during childhood according to the Moroccan national program of vaccination, was admitted in our unit for fever associated to mobile and transient arthritis and congestive heart failure.

Admission examination revealed a thin, unwell toxic-looking male, febrile (38.4°C), with tachycardia at 107 beats per minute and a normal blood pressure 120/70 mmHg. There was a grade 4/6 apical mitral regurgitant murmur but no splenomegaly or peripheral embolic phenomena, with no toxin-mediated manifestations.

The transthoracic echocardiogram (TTE), performed first, showed a non-mobile vegetation measuring 8 mm on the atrial side of the posterior mitral valve with moderate to severe mitral regurgitation. The transoesophageal echocardiography (TEE), performed the day after the admission, has confirmed the diagnosis.

Investigations revealed white cell count 17000/mm^3 (NR 4000-10000/mm^3) with 13900 mm^3 neutrophils (NR 2000-7000/mm^3). Hepatitis and HIV serology was negative. By day 5, two of four blood culture bottles taken before any antibiotic therapy, grew non-hemolytic, smooth, opaque colonies which were gram-positive coryneform bacteria. Metachromatic granules were demonstrated by Albert's staining technique and the organism produced characteristic black colonies on blood tellurite agar consistent with *Corynebacterium diphtheriae*. The strain was found to be non-toxigenic when tested by the guinea pig lethal test. The colonies were catalase positive, ferment glucose without gas production and do not produce urease or indole. The isolate was found to be sensitive to ampicillin, gentamicin, Ciprofloxacin, cefotaxime, vancomycin and imipenem, resistant to amikacin and showed intermediate sensitivity to penicillin G and ceftriaxon.

No metastatic septic emboli or peripheral aneurysm or pseudo-aneurysm formation were found on the systematic body scanner.

The patient received 12 g and 160 mg per day respectively of Opticillin and gentamicin (gentamicin was administered during 7 days) with a good clinical and biological improvement (apyrexia, normalization of white cell count and sterilization of blood culture).

However, at day 21 the patient developed a general allergic reaction to penicillin correctly jugulated with antihistaminic and corticoid therapy. After consulting the antibiotic susceptibility and in consultation with the advice of biologists, Penicillin was replaced by ciprofloxacin 1500 mg/24 hours in three doses for more 3 weeks. This incident had no impact on the results.

TTE and TEE control showed persistence of image of small vegetation with mild mitral regurgitation. The Minimum inhibitory concentration (MIC) of ciprofloxacin and the minimum bactericidal concentration (MBC) were not determined.

Discussion

C. *diphtheriae* endocarditis has been described as an aggressive and destructive disease, similar to Staphylococcus aureus endocarditis, with a high rate of complications [1].

As an example, over the past 10 years, five cases of infectious endocarditis due to nontoxigenic C. *diphtheriae* have been reported in Brazil. Four of these cases occurred in females aged 7-14 years. One case occurred in an adult over the age of fifty years. Of the child cases, one had congenital cardiac disease, one had recent undergone a major dental treatment and one had an episode of non-exudative pharyngitis

two weeks prior to the onset of infection. The mortality rate of these patients was 40% [4].

The C. *diphtheriae* endocarditis usually requires urgent surgical intervention, especially in patients with prosthetic valves. Most patients with C. *diphtheriae* endocarditis have underlying cardiac disease, prosthetic valves, or a history of intravenous drug use [5]. Cases in children and young adults with no other risk factors like in our patient have been reported [6].

'Diphtheroid' organisms are often regarded as contaminants when cultured in blood culture bottles, and the clinician must be aware of the possibility of invasive nontoxigenic C. *diphtheriae* disease. Some groups are recognized as being high risk for such infections.

Endocarditis as a result of this organism causes valvular destruction and valvular dysfunction, with frequent embolic complications and, in some, with the development of septic arthritis. It is characterized by large valvular vegetations, metastatic septic emboli with peripheral aneurysm and pseudoaneurysm formation and has a high mortality [5]. Our case illustrates only valvular dysfunction (moderate to severe mitral regurgitation) like previously reported in some cases [7].

Also, this case illustrated therapeutic problem caused by the allergic reaction to β-lactam and the use of ciprofloxacin which is rarely used against the C. *diphtheriae*. In most in vitro experiences, ciprofloxacin was effective on the C. *diphtheriae*. Although, in vivo studies showed reduced effectiveness of ciprofloxacin on the C. *diphtheriae*. Indeed, in a French series, the least active antibiotics were tetracycline, rifampicin and ciprofloxacin; The percentage of strains resistant to ciprofloxacin was 26% [8]. In our case, ciprofloxacin was used with good improvement remaining a valid therapeutic option against the strains of diphtheriae in Morocco.

Recommendations for medical treatment are based on expert opinion. It suggests that 4–6 weeks of a β-lactam antibiotic in conjunction with an aminoglycoside should be given which was applied for our patient [9]. Obviously if other agents are initially suspected, a broader cover is initially used. Treatment has been also successfully achieved with a cephalosporin and Gentamicin, penicillin alone and a cephalosporin with vancomycin [5]. Erythromycin and rifampicin also have useful activity against this organism [3]. When our patient developed the allergic reaction, β-lactam was substituted by ciprofloxacin to avoid cross-reaction with good improvement of the case.

Conclusion

This case underlines the efficiency of medical therapy (Penicillin or ciprofloxacin (even in-vivo) and Aminoglycoside) when *Corynebacterium diphtheriae* occurs on native valve with no major complication.

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