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CASE REPORT

An unusual case of native aortic endocarditis due to *Corynebacterium pseudodiphtheriticum*

Frédéric Wallet[1,2], Stéphanie Vanagt[3], Moulay Alaoui[4], Guillaume Gantois[5], Francis Juthier[2,6], Claire Duployez[1,2], Caroline Loïez[1,2]

[1,2]*Laboratoire de Bactériologie Hygiène, CHU Lille, Univ Lille Nord de France;*
[3]*Laboratoire de Biologie, Centre Hospitalier, Boulogne sur Mer;*
[4]*Service de Cardiologie, Centre Hospitalier, Boulogne sur Mer;*
[5]*Service d'Anesthésie-Réanimation, CHU Lille;*
[2,6]*Service de Chirurgie Cardiaque, CHU Lille, Univ Lille Nord de France*

SUMMARY

Corynebacterium pseudodiphtheriticum, a Gram-positive rod belonging the oropharynx microbiota, is usually described in pulmonary infections, especially in immunocompromised patients. This paper describes a rare case of native aortic infectious endocarditis (IE) and reviews the literature on similar cases. A 62-year-old man with rheumatic fever since childhood was hospitalized for surgical treatment of a febrile IE due *to C. diphtheriticum* with a large vegetation (15.8 X 8.3 mm). MALDI-TOF-MS from strain isolated in positive blood cultures identified *C. pseudodiphtheriticum* (2.34), and 16S rRNA sequencing from the valve sample confirmed the identification. The summary of 25 cases shows that the outcome of an IE due to *C. pseudodiphtheriticum* is bad. The review of the literature shows that this agent found in blood cultures in a cardiovascular context deserves to be explored meticulously because an unfavorable prognosis is frequent.

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INTRODUCTION

Corynebacterium pseudodiphtheriticum belongs to the skin microbiota and is a commensal bacterium of the nasopharynx (Fünke *et al*., 2007). In the majority of reported cases, *C. pseudodiphtheriticum* is responsible for pulmonary infections specially in immunocompromised patients suffering from respiratory tract diseases; other localizations are rare (Valdoleiros *et al*., 2020; Van Roeden *et al*., 2015). We describe a case of endocarditis due to *C. pseudodiphtheriticum* and review the literature on this pathogen in infective endocarditis (IE).

CASE REPORT

A 62-year-old man with paroxysmal atrial fibrillation, rheumatic fever since childhood, and a recently discovered diabetes was admitted to the cardiology department with asthenia and weakness in a febrile context beginning 15 days before. On initial examination, the patient presented with hyperthermia at 39.1°C. His pulse was irregular at 128 beats/min, and his blood pressure was 133/66 mmHg. Auscultation revealed a systolic-diastolic aortic murmur. No palpable spleen or peripheral cutaneous endocarditis symptoms were observed. Blood tests demonstrated a neutrophil leukocytosis (12.9x10^9/l with 81.9% of polymorphonuclears) and a high C-reactive protein concentration (107 mg/l). IE was suspected and transesophageal echocardiography confirmed the presence of a large vegetation (15.7x8.3 mm) on the aortic valve. Cerebral nuclear magnetic resonance showed multiple ischemic lesions without breaking the blood-brain barrier. Thoraco-abdominal CT performed showed two splenic embolizations. Six sets of separate blood cultures (Virtuo, bioMérieux, Marcy l'Etoile, France) were taken during the 48 first hours and treatment with amoxicillin (12 g/day), cloxacillin (12 g/day) and one shot of gentamicin (4 mg/kg) was begun. In light of this highly vegetated IE, the patient was transferred to the cardiac surgery ward for surgical treatment by biological valve replacement. The six aerobic blood culture bottles were positive after 42 hours of incubation. The direct examination of the smear showed a coryneform Gram-positive rod. Subcultures performed on blood agar incubated at 37°C in 5% CO_2 grew only a catalase-positive Gram-posi-

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Corresponding author:
F. Wallet M. D.
E-mail: frederic.wallet@chu-lille.fr

tive rod after 48 h of incubation. The bacteria were first identified by matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF-MS) with a Microflex mass spectrometer (Bruker Daltonik S.A., Wissembourg, France) according to the manufacturer's instructions after extraction by formic acid. With the Biotyper database containing 10694 main spectrum profiles corresponding to 3813 species, the result of the pattern matching process was expressed with a score of 2.34, giving *Corynebacterium pseudodiphtheriticum* as the most likely identification. A score higher than 2.0 was considered as identification at the species level by the manufacturer. *In vitro* susceptibility tests were performed using the disk diffusion method on Mueller-Hinton blood agar (Difco, Becton Dickinson, France) with 5% lysed horse blood. As recommended by CA-SFM (http://www.sfm-microbiologie.org), the breakpoints described for corynebacteria were used to determine the susceptibility of this bacterium. This strain was susceptible to amoxicillin (MIC by E-test=0.02 mg/l), clindamycin, vancomycin, trimethoprim-sulfamethoxazole, fluoroquinolones, linezolid, and rifampicin. The culture of the native sent to the laboratory was negative, but the identification of this agent was confirmed by 16S rRNA sequencing using primers described by Gauduchon *et al*. (Gauduchon *et al*., 2003). A fragment of 461 bp amplified from the valve sample and sequenced on an automated sequencer (377 ABI Prism; PE Applied Biosystems, Foster City, CA., USA) was compared with NCBI GenBank entries, giving 99% (460/461 bp) identity with *C. pseudodiphtheriticum* strain (GenBank accession no. URS00003F949C). As soon as the susceptibility of the bacterium was known, the antimicrobial treatment was reduced to amoxicillin (12 g/day). After treatment, the patient was quickly apyretic and echocardiography showed good functioning of the prosthesis after six weeks. A dental scan was performed to search the source of this bacterium but did not show any pathological lesion.

DISCUSSION

The review of the literature including key-words "*Corynebacterium pseudodiphtheriticum*" and "endocarditis" related few cases of IE due to *C. pseudodiphtheriticum*. Until 1991-1992, Morris *et al.* and Wilson *et al.* (Morris *et al*., 1991; Wilson *et al*., 1992) described 19 cases of IE due to *C. pseudodiphtheriticum* corresponding to 9 native valves and 10 prosthetic valves. For the native valves, patients had underlying heart disease in 7 out of 9 cases. Since this date, although the means of isolation and identification of corynebacteria using MALDI TOF-MS or molecular biology techniques have been developed, the literature reports only six additional cases of IE (*Table 1*). The summary of these 25 cases shows that the outcome of an IE due to *C. pseudodiphtheriticum* is bad (38% mortality for prosthetic valves to 50% for native valves). This Gram-positive rod belonging to the skin and oropharyngeal flora is often considered non-pathogenic. In case of positive blood culture with *C. pseudodiphtheriticum* and underlying cardiovascular pathology, the interpretation of a positive corynebacterium blood culture is not always easy. In cases of IE due to *Corynebacterium sp*, *C. pseudodiphtheriticum* is found less frequently than *C. striatum*, *C. amycolatum* and *C. jeikeium* (Bläckberg *et al*., 2021). While these last-mentioned species of corynebacteria are often resistant to beta-lactam agents, *C. pseudodiphthericum* remains sensitive to amoxicillin in the majority of the cases described, with one strain found resistant to penicillin and cephalosporins, requiring the use of vancomycin (Cauda *et al.,*1987).
The oropharyngeal flora remains the potential source of this infectious endocarditis. However, the dental scan performed on our patient did not show any pathological lesion to explain the source of this bacterium. Moreover, no skin lesions that could explain a potential origin of the translocation of this bacterium have been detected. On the pathophysiological level, Souza *et al*. (Souza *et al.,* 2015) showed *in vitro*

Table 1 - *Characteristics of IE due to C. pseudodiphtheriticum in the recent literature.*

Reference	*Age/Sex*	*Underlying condition*	*Valve*	*Diagnosis*	*Treatment*	*Outcome*
Rivero *et al*., 2003	62/F	Rheumatic fever	Aortic prosthetic	API gallery	Vancomycin + Gentamicin (allergy to penicillin)	cured
Johnson *et al*., 2014	14/M	Tetralogy Fallot	Pulmonary prosthetic	NR	Penicillin + Gentamicin Surgery	cured
Perez-Parra *et al.,* 2016	8/M	Bicuspid aortic valve	Aortic native	MALDI-TOF + 16S rRNA	Antibiotics Surgery (Ross)	died
Rasmussen *et al.*, 2020	79/M	NR	Aortic prosthetic	MALDI-TOF	Homograft	cured
Bläckberg *et al.,* 2021	NR	NR	NR	MALDI-TOF	NR	NR
Anton-Vasquez *et al*., 2022	81/M	NR	Aortic prosthetic	16S rRNA only	NR	NR

NR: not reported.

the ability of *C. pseudodiphtheriticum* to produce biofilm requiring an antimicrobial treatment for six weeks in case of IE.

CONCLUSION

C. pseudodiphtheriticum found in blood culture in an underlying cardiovascular patient deserves to be explored meticulously, especially since the prognosis of endocarditis due to this bacterium is often unfavorable.

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