Case Report

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Received 9 February 2014

Accepted 16 May 2014

Prosthetic valve endocarditis due to *Clostridium bifermentans*: a rare entity

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Introduction: Anaerobic endocarditis is clinically indistinguishable from aerobic causes of endocarditis. This necessitates correct identification of pathogens and determination of their antimicrobial susceptibility for adequate selection of antibiotic therapy effective against these organisms. *Clostridia* include anaerobic, spore-forming bacteria that cause a wide range of diseases and have been found to be associated with anaerobic endocarditis rarely.

Case presentation: We describe a case of prosthetic valve endocarditis in a 22-year-old man caused by *Clostridium bifermentans*. Infection was confirmed by culture and molecular identification of the bacterium. The patient was treated with antibiotic therapy with a favourable recovery.

Conclusion: Anaerobic bacteria are an uncommon but important cause of infective endocarditis and therefore correct diagnosis of rare species should not be ignored.

Keywords: Anaerobic; *Clostridium bifermentans*; endocarditis; prosthetic valve.

Introduction

Conventional microbiological identification of infection has generally been biased towards aerobes, and anaerobic infections tend to be neglected. Emerging molecular diagnostic methods hold promise to identify and isolate rare causes of infection rapidly. Here, we report a case of prosthetic valve endocarditis due to *Clostridium bifermentans* that was successfully treated, thus highlighting the importance of anaerobic causes of endocarditis in conventionally culture-negative individuals.

Case report

A 22-year-old male was seen in the Department of Cardiovascular Thoracic Surgery with past history of rheumatic heart disease with multivalvular dysfunction (moderate mitral stenosis, severe aortic stenosis and moderate aortic regurgitation). He had undergone double valve replacement in our hospital in May 2009, and remained asymptomatic for 3 months. In September 2009, he had fever, palpitations and dyspnoea. The echocardiography showed stuck aortic and mitral valves, and thrombolysis was attempted. The patient was not relieved of the symptoms and the thrombolysis was partially successful. Hence, in October 2009, a repeat thrombectomy was planned.

Investigations

His pre-operative investigations revealed that he was anaemic with a haemoglobin level of 8 g dl⁻¹, and his erythrocyte sedimentation ratio was raised (48 mm h⁻¹); other parameters of routine investigations were within normal limits. The blood cultures for aerobic, fungal and anaerobic organisms were sterile. A chest X-ray showed cardiomegaly with bilateral clear lung fields and two-dimensional echocardiography revealed stuck aortic and mitral valves with normal ventricular function. During the repeat thrombectomy, vegetations from both aortic and mitral valve hinges were removed and sent for aerobic and anaerobic culture, and normal movements of the valves were restored.

Diagnosis

The aortic and mitral valve vegetation did not yield any organism on aerobic and fungal culture. The aortic valve vegetation remained negative for anaerobic culture. However, the mitral valve vegetation yielded anaerobic growth after 48 h of anaerobic incubation on brain–heart infusion blood agar medium, showing grey-white to yellowish, circular, low convex colonies with slightly undulating margins and haemolysis. Growth was sensitive to a metronidazole disc (5 µg). On Gram staining,

Gram-positive bacilli were seen with oval, subterminal spores. The isolate was positive for indole production, aesculin hydrolysis, glucose fermentation, gelatin liquefaction and lecithinase production, and negative for nitrate reduction, lipase and fermentation of arabinose, maltose and salicin.

The isolate was identified as *C. bifermentans*, an anaerobe, by conventional identification methods and a rapid API 20A test (bioMérieux). It was later confirmed by PCR using broad-range 16S rRNA primers (Daly *et al.*, 1993) (Fig. 1) and sequencing. During the same period, the stool of the patient also grew *C. bifermentans* on anaerobic culture. Lymphadenopathy in the inguinal region was developed, and the biopsy sample grew methicillin-resistant *Staphylococcus aureus* but the blood culture did not.

Treatment

The patient was treated with intravenous antibiotics (vancomycin, and later linezolid, metronidazole, ciprofloxacin, amikacin and meropenem) for 21 days.

Outcome and follow-up

The post-operative period was uneventful, and during discharge he was put on oral antibiotics for the next 2 weeks and advised to attend for a follow-up visit after 1 week.

Discussion

C. bifermentans, although a saprophyte, has been reported to cause bacteraemia, septic arthritis and osteomyelitis in

humans (Chen *et al.*, 2001; Nolan *et al.*, 1972; Scanlan *et al.*, 1994). Endocarditis due to *Clostridium* spp. is rarely reported (Brook, 2008; Kolander *et al.*, 1989). Previously, *C. bifermentans* (Kolander *et al.*, 1989), *Clostridium histolyticum* (Durmaz *et al.*, 2000), *Clostridium septicum* (Cohen *et al.*, 1998) and *Clostridium endocarditis* (Holland *et al.*, 1997) have been reported. To date, only three cases of prosthetic valve endocarditis due to *Clostridium* spp. (*Clostridium perfringens*, *Clostridium clostridiformis* and *Clostridium limosum*) have been reported (Alvarez-Elcoro & Sifuentes-Osorio, 1984; Gordon & Axelrod, 1985; Robles *et al.*, 1997). Alvarez-Elcoro & Sifuentes-Osorio (1984) reported *C. perfringens* bacteraemia in a 23-year-old male patient with prosthetic valve endocarditis. The patient had undergone mitral and aortic valve replacement. The clinical data of endocarditis, signs of clostridial septicaemia and the presence of *C. perfringens* in all blood cultures suggested the diagnosis of infective endocarditis caused by *C. perfringens*. Gram-positive bacilli were also observed in a peripheral blood smear. Robles *et al.* (1997) reported prosthetic valve endocarditis and splenic abscess caused by *C. clostridiformis* in a 71-year-old male patient. The patient had an aortic prosthetic valve and *C. clostridiformis* was grown from three blood cultures. Gordon & Axelrod (1985) reported a patient with combined infection due to *Pseudallescheria boydii* and *C. limosum*. While *C. limosum* was grown in blood culture, both organisms were isolated from a surgically resected prosthetic aortic valve homograft (Gordon & Axelrod, 1985).

It has been a decade since the last report of prosthetic valve endocarditis due to a *Clostridium* sp. Here, we have reported the first case, to our knowledge, of prosthetic mitral valve endocarditis due to *C. bifermentans*. This report highlights the importance of awareness in the medical fraternity regarding the anaerobic causes of endocarditis, in order to look for anaerobes especially in conventional culture-negative individuals. There is a need for rapid and accurate identification system for such anaerobes, such as the API 20A test. Molecular diagnostic techniques like PCR and sequencing help to characterize the rarer isolates and distinguish *C. bifermentans* from the related *Clostridium sordellii* and *Clostridium difficile*, a known nosocomial pathogen. The likely portals of entry in cases of clostridial endocarditis include the oropharynx, skin, and gastrointestinal and genitourinary tracts (Felner & Dowell, 1970). In the present case, the gastrointestinal tract was the probable portal of entry.

Anaerobic endocarditis accounts for 2 % of native valve and 3 % of prosthetic valve infections (Gentry & Khoshdel, 1989; Brook, 2008) and is indistinguishable clinically from aerobic endocarditis (Felner & Dowell, 1970). Hence, laboratory diagnosis for an anaerobic aetiology should be sought in all cases. Cardiac sequelae such as congestive heart failure, arrhythmias and cardiogenic shock are reported in anaerobic endocarditis (Felner & Dowell, 1970). We have reported a case of constrictive pericarditis due to an anaerobe (*C. sordellii*) previously (Chaudhry *et*

Fig. 1. Results of a broad-range PCR assay. The band corresponding to the 330 bp sequence of the 16S rRNA gene of members of the genus *Clostridium* is indicated (arrow). Lane 1, 100 bp ladder (MBI Fermentas); lane 2, mitral valve isolate; lane 3, stool isolate; lane 4, *C. difficile* ATCC 9689 reference strain used as a positive control; lane 5, negative control.

al., 2011). Awareness in both clinicians and microbiologists is required for correct diagnosis as well as timely and proper management of the patient.

Acknowledgements

We acknowledge the help of the CTVS team at AIIMS who looked after this patient and Dr Amita and Mr V Arvind for their help. The authors have no conflicts of interest to disclose.

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