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SHORT REPORT

Prosthetic valve endocarditis with aortic root abscess due to *Achromobacter xylosoxidans* subsp *denitrificans* – A rare case report

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Abstract

A young patient with congenital aortic stenosis and aortic valve replacement developed Prosthetic valve endocarditis (PVE) and aortic root abscess due to *Achromobacter xylosoxidans* subsp. *denitrificans*. PVE with this organism is rare and only 1 case has been reported in the literature. Our patient had an uneventful recovery with appropriate antibiotic therapy.

Key words

Endocarditis, Bacterial; Heart valve prosthesis and microbiology; *Achromobacter denitrificans*

Introduction

Despite recent advances in cardiovascular surgical techniques, Prosthetic valve endocarditis (PVE) continues to complicate the recovery of a small percentage of patients after cardiac valve replacement.[1] PVE has been estimated to occur with a relatively low but increasing frequency ranging from 0.1% to 2.3% per patient-year and to account for 1-5% of all cases of acute infective endocarditis (AIE).[2] Usually, PVE is associated with aortic root abscess.[3] It is a time related event classified into early and late. Early infections are acquired following intra-operative or post-operative contamination of the valve, which is usually nosocomial in nature. Late infections also have been attributed to contamination of the valve. An incidental infection or trauma to body surfaces colonized with microorganisms resulting in bacteraemia is probably the source of the valve infection.[2] Microbiology of PVE

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depends on the time of onset of endocarditis following the valve replacement. Approximately 40-60% of early onset PVE is caused both by Gram positive cocci and Gram negative bacteria.

PVE, with the non fermenting Gram negative rod, *A. xylosoxidans* subsp. *denitrificans* is a rare and an unusual entity.[3] This emerging pathogen, previously termed as *Alkaligenes xylosoxidans,* is a motile, oxidase positive, non fermenting Gram negative rod. It is ubiquitous and widely distributed, usually in the aquatic environment.[4] In spite of its low virulence and intrinsic pathogenicity, *A. xylosoxidans* subsp *denitrificans* acts as an opportunistic pathogen and causes serious clinical infections, including PVE, in immunocompromised patients. We herein report a case of PVE with aortic root abscess.

Case Report

A 17 year old boy, a known case of congenital heart disease (CHD) with aortic stenosis had undergone aortic valvotomy during his childhood. Later, aortic valve replacement was performed in May 2011 in our Institute for severe aortic regurgitation. One month later, the patient experienced intermittent episodes of low grade fever. In October 2011, he presented with high grade fever and was readmitted and investigated further with a clinical suspicion of early onset PVE.

Three sets of blood cultures, BacT/Alert FAN aerobic & standard aerobic bottle per set (*bioMerieux, Marcy l' Etoile* France) were submitted to the microbiology lab within 24 hours of admission. All the 3 sets flagged positive with a mean time to detection of 21.8 hours. The bacterial isolate from these culture bottles was identified as *A. denitrificans*, as described later. Based on the blood culture report, a 12th hourly intravenous antibiotic therapy was initiated with meropenem 500mg and levofloxacin 500mg.

A trans-esophageal echocardiographic (TEE) findings revealed a mechanical prosthetic valve that was partially dehisced and unstable. An abscess was detected posterior to the aortic root with mild peri and paravalvular leak. A redo aortic valve replacement was performed on 21st October 2011.

The surgically debrided valve tissue was submitted for culture, which also yielded *A. xylosoxidans* subsp. *denitrificans,* with similar susceptibility pattern as the blood culture isolate. A post-operative 2D echo, after 15 days was reported to be normal with good functioning of the aortic valve and with no leaks. Levofloxacin was discontinued and the patient was continued on meropenem and oral co-trimoxazole DS (160mg trimethoprim and 800mg sulfamethoxazole) was added for the next two weeks (a total of 4 weeks

Figure 1. Colony morphology of *Achromobacter denitrificans* on 5% sheep blood agar and chrome agar

1-2 mm smooth, circular, moist colonies with distinct orange to yellow pigmentation

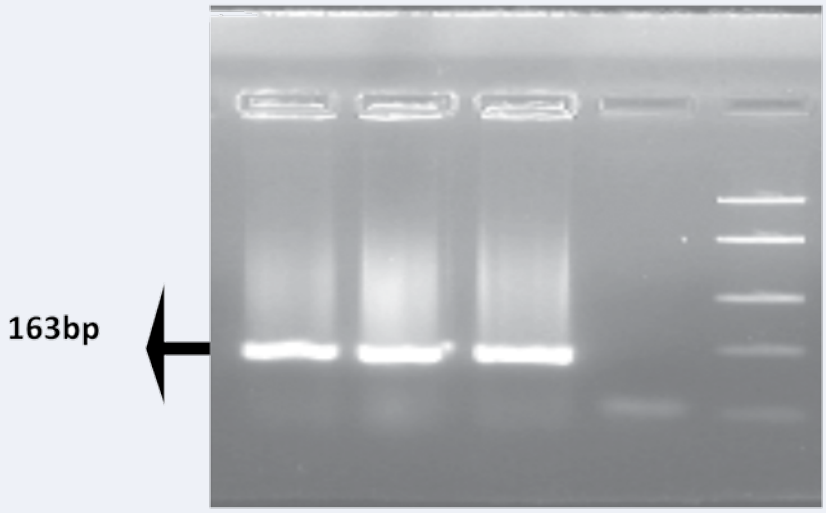

Figure 2. Agarose gel electrophoresis of PCR products to confirm *A. denitrificans* isolates-Genus specific band at 163 bp

Lane M: Marker-100 bp ladder

Lane 1: *P. aeruginosa* ATCC 27853 (negative control)-no band at 163 bp

Lane 2: *A. denitrificans* isolate from Blood culture, B15384-band at 163 bp

Lane 3: *A. denitrificans* isolate from Blood culture, B15954-band at 163 bp

Lane 4: *A. denitrificans* isolate from cardiac valve, E7147-band at 163 bp

of antibiotic therapy post surgery). He responded gradually to this prolonged antibiotic therapy and was clinically stable at the time of discharge.

Microbiology workup

The isolate from the blood cultures and valve tissue was a Gram negative non-fermenting rod that grew on both blood agar and chrome agar (COS & CPS, *bioMerieux, Marcy l' Etoile* France) aerobically at 37ºC by 48 hours, on subculture. Morphologically, the colonies were 1-2mm smooth, circular, moist colonies with distinct orange to yellow pigmentation, on both the plates (figure 1). The organism was oxidase and catalase positive, non motile and was identified as *A. xylosoxidans* subsp *denitrificans* with ID-GN panel of the Vitek 2 system and the ID 32 GN panel of the mini API (*bioMerieux,Marcy l' Etoile* France) as a non-fermentor. Antimicrobial susceptibility testing was performed with N090 panel of the Vitek 2 system and ATB PSE (5) of the mini API. The isolate was susceptible to co-trimoxazole, ciprofloxacin, levofloxacin, imipenem, meropenem, ceftriaxone and piperacillin-tazobactam.

A Polymerase Chain Reaction (PCR) was performed on three isolates of *A. xylosoxidans* subsp. *denitrificans* (two from blood cultures and the one from valve tissue). *Pseudomonas aeruginosa (ATCC 27853)* was used as a negative control. Species specific 16S rRNA and 163bp primers for *A. xylosoxidans* subsp. *denitrificans* were used.[5] The bacterial DNA was extracted by the TEX protocol[6] and amplified using the primers: AX-F1 GCAGGAAAGAAACGTCGCGGGT and AX-B1 ATTTCACATCTTTCTTTCCG..

The PCR reaction mixture contained in 20µl reaction volume contained 2µl of template, 2.5U of *Taq* polymerase, 150µ*M* of dNTP (both reagents were supplied by Board of Radiation and Isotope Technology, Jonaki Regional Centre, Hyderabad), 1x PCR buffer (Fermentas) containing 1.5*mM* $MgCl_2$ and 20 *pmoles* of each primer. The amplification was performed under the following conditions: 94ºC for 5 min, 40 cycles of 94º C for 30s, 54º C 1 min, 72º C for 1 min and final extension 72º C for 10 mins. The amplicons were analyzed on 1.5% agarose after staining with ethidium bromide and documented in Alfa Imager Inc trans illuminator photo documentation system. 163 bp product was detected in all the isolates

of *A. xylosoxidans* subsp *denitrificans* as described by Lixia Liu *et al.*[5] (figure 2), confirming the genotype of the 3 *A. xylosoxidans* subsp *denitrificans* isolates from the patient. There was no amplification of *P. aeruginosa* DNA (figure 2).

Discussion

The genus *Achromobacter* was earlier named as *Alcaligenes*. The recent 16S rRNA sequence analysis and GC content studies of the organism support its nomenclature as genus *Achromobacter* with two subspecies, *A. xylosoxidans* subsp. *xylosoxidans* and *A. xylosoxidans* subsp. *denitrificans*.[7]

This organism is a ubiquitous environmental, aerobic, oxidase positive, non-glucose fermenting, Gram negative rod initially characterized by *Holmes* and further studied and named by Yabuuchi and Ohyama in 1971 from 7 patients with chronic otitis media.[8] It is a relatively uncommon human pathogen, capable of causing invasive infections in both immunocompetent and immunocompromised hosts. Healthcare associated infections predominate with an association between infection and immunosuppression, especially in patients with underlying malignancies, neutropenia, bone marrow or liver transplantation, diabetes mellitus, renal failure, cystic fibrosis, HIV infection, IgM deficiency, neonates and healthy individuals. Reports on clinical infections by this pathogen are rare from India.

The most common manifestation of infection documented with this organism is bacteremia, with a mortality rate of more than 50%. PVE, usually develops between 4-6months of valve replacement due to *Achromobacter xylosoxidans* subsp *denitrificans*[9] as also seen in our case. While PVE due to *Achromobacter xylosoxidans* subsp *xylosoxidans* has been reported in few cases[3,8,10,11] we found only one reported case of PVE due to *Achromobacter xylosoxidans* subsp *denitrificans*.[9]

The other documented clinical manifestations of infections caused by this pathogen include primary bacteremia, pneumonia, renal abscess,[12] prosthetic valve endocarditis, cholecystitis, peritonitis, keratitis[13] and meningitis.[14]

Characteristic antimicrobial susceptibility patterns of *A. xylosoxidans* subsp. *denitrificans* include high levels of resistance to aminoglycosides, narrow spectrum penicllin, first and second-generation cephalosporins and some third generation cephalosporins (cefatoxime and ceftriaxone). *A. xylosoxidans* subsp. *denitrificans* is generally susceptible to ceftazidime, extended spectrum penicillins, carbapenems and sulphonamides where as susceptibility to quinolones is variable.[9,12]

Though the most appropriate antimicrobial therapy has not been determined against *A. xylosoxidans* subsp. *denitrificans,* levofloxacin, meropenem and co-trimoxazole were effective in our patient, as was also the experience in other studies. Our isolate was sensitive to ceftriaxone, cotrimoxazole, quinolones, carbapenems and colistin. Identification of *A. xylosoxidans* subsp. xylosoxidans may be problematic as traditional phenotypic and commercially available tests are often unreliable and may lead to misidentification as other non-fermenting organisms, in particular with members of the *Burkholderia cepacia* complex. Molecular methods such as PCR and sequencing of ribosomal genes allow for more accurate identification of non-fermenting Gram-negative rods than traditional phenotypic methods.[3,5,7] The PCR, using *A. xylosoxidans* subsp. *denitrificans* specific primers, confirmed the identification and the relatedness of the 3 isolates of *A. xylosoxidans* subsp. *denitrificans* (from blood and valve tissue).

Risk factors for higher mortality rates in infections with *A. xylosoxidans* include age over 65 years, neutropenia, presence of poly-microbial infection and nosocomial infection.[9] After extensive search, we could not find the source of the infection in our patient. Our patient was an otherwise well preserved young boy with no co-morbid or immunosuppressive states. Except for surgery there was no other risk factor for acquiring infection with an uncommon and unusual pathogen like *A. xylosoxidans* subsp. *denitrificans*. It is probable that the patient acquired the valve infection either intra-operatively or postoperatively. Hence, strict infection control measures including care of prosthetic devices should be in place to prevent such infections.

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