Late aortic prosthetic valve endocarditis due to *Achromobacter xylosoxidans* infection: a case report and review of the literature

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**ABSTRACT:**

*Background:* Prosthetic valve endocarditis (PVE) represents a life-threatening infection that may complicate valve replacement, associated with high morbidity and mortality. There is no clinical presentation characteristic of PVE. Causative agents of community-acquired PVE include endogenous microbiota, such as *viridans* group streptococci and enterococci, similar to native valve endocarditis etiology. An increasing number of recent publications have addressed the pathogenic role of *Achromobacter xylosoxidans*, a causative agent of a wide range of opportunistic infections in immunocompromised patients and healthcare-associated infections. However, it has only rarely been associated with the development of endocarditis, most commonly reported in patients with severe immune impairment caused by various pathological conditions or in very frail elderly patients.

*Case presentation:* A severe aortic valve graft infection by *A. xylosoxidans* is described with a literature review. A 69-year-old man with multiple serious comorbidities developed severe aortic endocarditis due to *A. xylosoxidans* after aortic valve replacement surgery. Only treatment with daptomycin, gentamicin and ampicillin allowed to obtain long-term clinical improvement.

*Conclusions:* An extensive review of the literature on cases of *A. xylosoxidans* endocarditis was conducted. Our review highlights that PVE due to *A. xylosoxidans* has a high mortality.

*Keywords:* *Achromobacter xylosoxidans*, *Achromobacter* species, Prosthetic valve endocarditis, Endocarditis.

**INTRODUCTION**

*Achromobacter xylosoxidans* (AX), previously known as *Alcaligenes xylosoxidans*, is a non-fermenting, catalase- and oxidase-positive, gram-negative, flagellate bacterium. It has been named *xylosoxidans* due to its ability to easily oxidize xylose and glucose. It shows an unpredictable profile of *in vitro* antibiotic susceptibility tests, with resistance to aminoglycosides and variably resistance to quinolones and trimethoprim-sulfamethoxazole. The organism exists in a water environment and is a common contaminant of fluids. In human bodies, it may be part of the normal endogenous microbiota of the ear canal, the skin, and the gastrointestinal tract. It can form biofilms on plastics treated with disinfectant solution, including medical products.

In some settings, some antiseptics and disinfectants do not eliminate biofilm-forming Gram-negatives *Achromobacter* spp., becoming a source of pathogen transmission and possible consecutive outbreaks of healthcare-associated infections.
Since its recognition, it has been documented in literature to cause a wide range of infections. In recent years, it has been isolated with increasing frequency in the hospital setting, especially among immunocompromised patients and carriers of indwelling catheters. The most common clinical pictures include bacteremia, pneumonia, biliary tract infection, urinary tract infection, wound infection, and peritonitis. We conducted a search of English-language records of A. xylosoxidans endocarditis through MEDLINE, from 1952 to December 2022, using MeSH “Achromobacter” and “endocarditis”; until now, only 30 other cases of infective endocarditis (IE) caused by AX infection have been reported. Our review highlighted the importance of the existing valvular heart disease as a predisposing factor, which existed in more than 80% of the reported cases (Supplementary Table 1 and Supplementary Table 2). In addition, patients with diabetes mellitus and chronic renal failure or intravenous drug users may also represent at-risk populations for developing A. xylosoxidans endocarditis. Of the reported cases of A. xylosoxidans endocarditis, three of them, involving the mitral valves, were observed in patients with end-stage renal disease (ESRD) on hemodialysis (HD), expiring despite antibiotic treatment, although two of the three patients received valve replacement.

Diabetes mellitus was detected in 8 patients, 5 of whom died, but in the case described by Kumar et al. in a dialysis patient, the outcome was not reported. Intravenous drug use was detected in three male patients, two of whom recovered with antibiotic and surgical therapy, while the outcome of the third patient was not reported; one of these patients presented multiple right aortic root abscesses and prosthetic valve endocarditis (PAVE), while a second patient had prosthetic mitral valve endocarditis (PMVE) and finally the third patient presented a tricuspid valve endocarditis (TVE). The latter was initially treated with antibiotics and then was transferred to a medical center for surgical intervention, but was lost to follow-up.

The existence of a state of immunodeficiency favored the infection in three patients, two of whom died, while the outcome was not described for the third. Martino et al. reported a fatal hospital-acquired catheter-related right-sided IE and pulmonary embolism in a 33-year-old male with myelofibrosis and bone marrow transplantation. Patel et al. described a fatal septiceptic aortic valve endocarditis (AVE) and mitral valve endocarditis (MVE) in a 72-year-old female affected by granulomatosis, treated with steroid and azathioprine. A MVE with microabscesses and pneumothoraces in a 67-year-old asplenic male with rheumatic heart valvular disease (RHVD), has also been documented, without other information about his outcome.

Only four cases occurred on native valves without structural abnormalities (three cases involved the mitral valve and aortic valve, and one case involved only the mitral valve), while prosthetic valve endocarditis (PVE) was recognized in nine patients, including our case (Supplementary Table 1).

Out of the 30 patients with AX IE, most of the cases was involved the aortic valve. A unique challenge posed by AX infection is the inherent resistance to most aminoglycosides, first and second-generation cephalosporins, and the variable resistance to fluoroquinolones. According to the existing literature, surgical and medical therapy may need to be combined. However, the optimal therapeutic regimen for treating AX endocarditis remains unclear because of the limited data.

We herewith discuss a rare case of AX PVE, nine years after heart surgery for aortic artery dissection. This case is the first AX infection of aortic graft reported in an Italian patient. We also provide a review of case reports of IE due to Achromobacter species (spp.) and AX infection published in the English literature, through a Pub Med/MeDline search and the subsequent review of noted references.

**CASE REPORT**

A 69-year-old obese male suffering from blood hypertension and type 2 diabetes mellitus was moved to our ward from a reference centre of heart surgery, where an aortic composite valve graft replacement was performed after a type A aortic dissection, according to Bentall’s procedure. Both transesophageal heart ultrasonography and thorax angio-CT scan demonstrated a severe prosthetic paravalvular leak and aortic valve graft vegetations, and positron-emission tomography (fluorodeoxyglucose-PET) showed pathological accumulations in the same area.

Laboratory examinations showed a frank leukocytosis with neutrophilia (16,070 and 13,949 cells/µL, respectively), and a serum C-reactive protein level of 128.7 mg/L (normal range value, 0-5 mg/L).

Blood cultures resulted positive for AX; the antimicrobial susceptibility testing highlighted resistance to most of penicillins-cephalosporins derivatives and tigecycline, while carbapenems, quinolones and aminoglycosides tested sensitive. The initial empiric therapy based on piperacillin-tazobactam, followed by intravenous (iv) vancomycin-imipenem-rifampicin, was switched to iv daptomycin-gentamicin-high-dose ampicillin, also due to the worsening kidney function. Later, upon the improvement of all clinical, laboratory, and instrumental parameters, discharge became possible with long-term cardiological follow-up.

**DISCUSSION**

PVE is a well-studied morbid condition that accounts for 10% to 30% of all cases of IE. PVE is a serious potential complication of valve replacement surgery with significant mortality.

In fact, PVE complicates the clinical course of 1-6% of patients with prosthetic valves, and it is one of the types of IE with the worst prognosis. It occurs at the rate of 0.3-1.2% per patient-year in surgical aortic valve replacement (SAVR) and carries significant morbidity/mortality.
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The incidence and risk of PVE after SAVR are higher in patients with biological valves compared to those with mechanical valves.

The type of prosthetic heart valve is associated with the causative pathogen, since different bacteria predominantly adhere to different types of valve materials.

Patients with mechanical valve prostheses have a higher risk of having Staphylococcus aureus PVE compared to patients with bioprosthetic valves. On the contrary, patients with bioprosthetic valves are more likely to have a-hemolytic streptococci PVE. Berisha et al. found no statistically significant difference in the distribution of causative pathogens depending on aortic or mitral localization. This was also the case when comparing early and late PVE.

According to the English literature, there have been 30 cases of Achromobacter spp. IE described to date, with most of the cases having prior cardiac surgeries or severe premorbid valve disease; patients’ characteristics are reported in Supplementary Table 1.

In this series, most strains were isolated from hospitalized patients with severe underlying diseases, who had been subjected to various invasive procedures and given a wide range of chemotherapeutic agents.

A prosthetic valve was involved together with bacteremia in nine cases, including our case; also, 20 cases reported native valve infection. A review of the English language literature on well-documented AX PVE is summarized in Supplementary Table 2.

Of the nine PVE caused by AX, five were females and four males, with a median age of 58.3 and a range of age between 35 and 86. The most frequent underlying diseases were cardiac diseases, followed by diabetes mellitus and chronic renal failure; two patients had a history of intravenous drug use. Four patients died – two females, and two males, with a median age of 66.7, range of age 35-86. Of these, three patients were older than 69 years. On the contrary, five patients, two males and three females, with a median age of 51.6 (range of age: 37-68), survived and recovered; three patients were aged >54 years.

AX infections are challenging to treat due to the reduced effectiveness of a wide range of antimicrobial agents; in vitro susceptibility data showed that most isolates were usually susceptible to meropenem, trimethoprim-sulfamethoxazole, and piperacillin/tazobactam. Xia et al. described the first reported Achromobacter endocarditis that developed resistance to meropenem in a 66-year-old female with MVE, with associated abscess and septic emboli in the cerebellum and the psoas muscle at autopsy. Overall, ampicillin, meropenem, piperacillin/tazobactam, and cotrimoxazole appeared to be the most dependable drugs for treatment.

A diagnosis of pacemaker-lead endocarditis due to AX was made in a 35-year-old patient who had undergone a patch closure of the ventricular septal defect 18 years before. The patient was successfully treated with a prompt surgical removal of the entire pacing system and antimicrobial therapy based on the antimicrobial susceptibility testing was administered.

Another report of right-sided infective endocarditis and intracardiac abscess with a cutaneous fistula and sternal wound discharge was caused by AX; it occurred many years after the repair of a perimembranous ventricular septal defect (VSD). The patient was treated with intravenous piperacillin/tazobactam for eight weeks and was prescribed trimethoprim/sulfamethoxazole two times daily indefinitely, for suppression of bacterial activity.

Another rare presentation of native valve IE was noted in a 72-year-old female with recurrent knee septic arthritis and fatal sepsis affected by granulomatous polyangitis treated with steroids and azathioprine. Moreover, a rare case of a Hickman catheter-related bacteremia, right-sided IE, and pulmonary embolism diagnosed after a bone marrow transplantation has been recorded from Italy.

Of interest, we found a few cases in the literature reporting AX IE in the New Zealand white rabbits and in one dog.

**CONCLUSIONS**

Clinicians should be aware of this emerging gram-negative pathogen; although intrinsically poorly virulent, it may be responsible for local, complicated clinical pictures, sometimes leading to repeated heart surgery or patient death.
The present case and a review of the current literature demonstrate the emergence of AX as a potential pathogen, not only in immunocompromised individuals but in any patient with an indwelling catheter and in patients with cardiac valvular disease. According to the literature search, early intravenous antibiotics and immediate surgical management need to be promptly combined, because a combination approach is considered appropriate and crucial for a favorable outcome.

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