Achromobacter species endocarditis: A case report and literature review

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Endocarditis due to *Achromobacter* species is a rare, yet serious, endovascular infection. *Achromobacter* species infective endocarditis is associated with underlying immunodeficiencies or prosthetic heart valves and devices. A case of prosthetic pulmonary valve endocarditis secondary to *Achromobacter xylosoxidans* subspecies *denitrificans* is described in the present report. This life-threatening infection was successfully treated with combined valve replacement and prolonged antibiotic therapy. A Medline/PubMed literature review of *Achromobacter* endocarditis was also performed. *Achromobacter* species are an uncommon, yet important, cause of nosocomial endocarditis. Given the significant associated morbidity and mortality, along with a high degree of intrinsic antibiotic resistance, *Achromobacter* species infective endocarditis remains a clinical treatment challenge.

Key Words: Achromobacter xylosoxidans *subspecies* denitrificans; Alcaligenes xylosoxidans; *Infective endocarditis; Nosocomial*

L'endocardite à espèces d'*Achromobacter* : un rapport de cas et une analyse bibliographique

L'endocardite causée par des espèces d'*Achromobacter* est une infection endovasculaire rare, mais grave. L'endocardite infectieuse à espèces d'*Achromobacter* s'associe à des immunodéficiences sous-jacentes ou à des valves et dispositifs cardiaques prosthétiques. Le présent rapport décrit un cas d'endocardite de la valve pulmonaire prosthétique secondaire à un *Achromobacter xylosoxidans* de sous-espèce *denitrificans*. Cette infection mettant en jeu le pronostic vital a été traitée avec succès par une association de remplacement valvulaire et d'antibiothérapie prolongée. Les chercheurs ont également procédé à une analyse bibliographique de l'endocardite à *Achromobacter* dans Medline et PubMed. Les espèces d'*Achromobacter* sont des causes peu courantes, mais importantes, d'endocardite nosocomiale. Étant donné la morbidité et la mortalité connexes marquées et le fort degré d'antibiorésistance intrinsèque, l'endocardite infectieuse à espèces d'*Achromobacter* demeure un défi thérapeutique clinique.

Although frequently encountered in aquatic environments, *Achromobacter xylosoxidans* is an uncommon source of bloodstream infections in humans (1-3). *A xylosoxidans* is of epidemiological significance due to its role as a hospital pathogen, its antimicrobial resistance profile and its implication in outbreaks (4). Because *A xylosoxidans* endocarditis is rare, few cases have been reported in the literature. We report a patient with endocarditis caused by *A xylosoxidans* subspecies *denitrificans*, and provide a literature review of *Achromobacter* species endocarditis.

CASE PRESENTATION

A 54-year-old African-American woman with tetralogy of Fallot initially underwent a Blalock-Taussig shunt placement as a child, followed by total repair as a teenager. Due to valvular insufficiency, the patient required a bovine pulmonary valve replacement. Four months later, she was admitted to hospital #1 with a fever of 39.5°C, tachycardia, hypotension and leukocytosis. On admission and eight days later, her blood cultures grew *A xylosoxidans*. Using the Microscan WalkAway 40 System (Siemens Healthcare Diagnostics Inc, USA), the isolates were found to be susceptible to cefepime, ceftazidime, ciprofloxacin, imipenem, levofloxacin, piperacillin/tazobactam, ticarcillin/clavulanate and trimethoprim/sulfamethoxazole; intermediately susceptible to ceftriaxone; and resistant to amikacin, aztreonam, gentamicin, tetracycline and tobramycin. Given her complicated anatomy, the patient was transferred to a tertiary care facility for further management. She was initially treated with both piperacillin/tazobactam 4.5 g intravenously every 6 h and levofloxacin 750 mg intravenously daily. Additional work-up included a computed tomography angiography of the chest revealing a right-sided pulmonary embolus and airspace disease in the right middle and lower lobe. A transesophageal echocardiogram revealed a 2.7 cm × 2.2 cm echodensity on the prosthetic pulmonic valve, with moderate to severe stenosis and a preserved ejection fraction. A peripherally inserted central catheter was placed after confirming negative blood cultures, and she continued piperacillin/tazobactam for six weeks.

Approximately one week after completing the antibiotic therapy, the patient was readmitted to a neighbouring hospital, hospital #2, with heart failure, abdominal pain and fever. Blood cultures, obtained four days apart, grew *A xylosoxidans*; susceptibility testing was not performed on these isolates. The patient was transferred back to the tertiary care facility. Repeat blood cultures performed at our hospital nine days later grew *A xylosoxidans* subspecies *denitrificans*. Antibiotic susceptibilities were determined using the Vitek 2 System (bioMérieux Inc, USA). The organism was susceptible to ampicillin/sulbactam, imipenem, ceftazidime, piperacillin/tazobactam, levofloxacin, ciprofloxacin and trimethoprim/sulfamethoxazole; intermediate to amikacin, cefepime, tobramycin and gentamicin; and resistant to cefazolin, cefoxitin, ceftriaxone and aztreonam. Piperacillin/tazobactam was again prescribed, and blood cultures obtained two days later were negative. A repeat transesophageal echocardiogram revealed a 2.4 cm × 1.4 cm vegetation on the pulmonic valve, with moderate to severe stenosis and an ejection fraction of 70%. A computed tomography scan of the abdomen and pelvis revealed the presence of splenic infarcts, hepatomegaly, dilated right atrium and hepatic veins, and diffuse periportal edema. After consultation with the infectious diseases department, the antimicrobial regimen was changed to imipenem/cilastatin 500 mg intravenously every 8 h.

Surgery was deferred secondary to rectal bleeding, fever, hypotension and respiratory distress. Repeat blood cultures obtained eight days after starting imipenem/cilastatin therapy grew *A xylosoxidans* subspecies *denitrificans*, with no change in the antibiotic susceptibility pattern. Due to the persistence of the bacteremia, 750 mg of intravenous

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TABLE 1
***Achromobacter* species endocarditis**

Reference	Age (years), sex	Organism	Comorbidities	Clinical presentation	Treatment	Outcome
Present case	54, female	*Achromobacter xylosoxidans* subspecies *denitrificans*	Tetralogy of Fallot with prosthetic pulmonary valve	PV endocarditis, pulmonary embolus, splenic infarcts	Piperacillin/tazobactam, imipenem/cilastatin, levofloxacin; surgery	Recovered
7	50, male	*A xylosoxidans*	Dialysis	MV endocarditis	Amoxicillin/clavulanic acid, additional 'broad-spectrum' antibiotics not defined; surgery	Died
8	69, male	*A xylosoxidans*	Diabetes, dialysis, cardiovascular disease, AVR	MV and AV endocarditis with liver, spleen, kidney infarcts and abscesses	Ciprofloxacin, ceftazidime, ertapenem, tigecycline, TMP-SMX; surgery	Died
9	37, male	*A xylosoxidans* subspecies *xylosoxidans*	Intravenous drug user, AVR	AV endocarditis with aortic root abscesses	Meropenem; surgery	Recovered
10	35, male	*A xylosoxidans*	VSD patch repair and pacemaker	Pacemaker lead and RV outflow tract endocarditis	Ceftazidime, piperacillin; surgery	Recovered
11	46, male	*A xylosoxidans*	Diabetes, ischemic stroke, s/p lobectomy for emphysema	AV and MV endocarditis	Ampicillin/sulbactam, TMP-SMX; surgery	Recovered
12	33, male	*A xylosoxidans*, *Candida* species	Myelofibrosis, s/p bone marrow transplant	Right atrial thrombus, pulmonary embolus	Aztreonam, amikacin	Died
13	30, male	*A xylosoxidans*	Heart failure	AV endocarditis	None	Died
14	77, female	*A xylosoxidans*	AVR	MV and AV endocarditis with retinal hemorrhage	Tobramycin, carbenicillin, TMP-SMX, moxalactam	Died
15	35, male	*A xylosoxidans*	AVR	Sinus tract from mediastinum to aortic prosthesis, cerebral embolus	Carbenicillin, TMP-SMX, rifampin, moxalactam, azlocillin	Died
16	20, male 4, male	Unidentified *Achromobacter* species	Tetralogy of Fallot repair with Ivalon patch, congenital interventricular septal defect	Not stated	Penicillin, streptomycin, novobiocin, chloramphenicol, triple sulfonamide, sulfadiazine; surgery in surviving patient	1 died, 1 recovered
17	28, male	*Achromobacter* group B	AVR	AV endocarditis	Cefuroxime, gentamicin	Recovered

AV Aortic valve; AVR AV replacement; MV Mitral valve; PV Pulmonic valve; s/p Status post; RV Right ventricle; TMP-SMX Trimethoprim/sulfamethoxazole; VSD Ventral septal defect

levofloxacin given daily was added, and the imipenem/cilastatin dose was increased to 500 mg intravenously every 6 h. The next set of blood cultures obtained six days later was negative. One month into her second admission, the patient underwent pulmonic valve replacement. Intraoperatively, complete dehiscence of the prosthetic pulmonary valve was observed. Additionally, the patient required debridement of an anterior mediastinum and pulmonary outflow tract abscess. Histopathology of the valve was consistent with acute endocarditis; however, tissue Gram stains and cultures were negative for any pathogens. She had an uneventful postoperative recovery and received an additional four weeks of intravenous imipenem/cilastatin therapy. To our knowledge, the patient experienced no recurrence of infection within the six-month postoperative period.

METHODS

A literature review of *A xylosoxidans* endocarditis was performed using the Medline/PubMed database. Only articles published in English were considered. A search using the terms "Achromobacter" and "endocarditis" yielded 14 articles. A separate search using the terms "Alcaligenes" and "endocarditis" yielded 21 articles. Due to various changes in taxonomy over the past few decades, it was opted to include cases secondary to *Achromobacter* group B and unidentified *Achromobacter* species in the present review of *A xylosoxidans* endocarditis. References from pertinent articles were reviewed to identify additional cases. Two cases were not published in English and were, thus, not reviewed (5-6). A total of 11 articles and 12 case reports were identified (7-17) (Table 1). All cases were reported between 1960 and 2009.

DISCUSSION

A xylosoxidans is an aerobic, motile, oxidase-positive, nonfermenting, Gram-negative rod bacterium found in aquatic environments (18). It was first described in 1971 after being cultured from the purulent discharge of seven patients with chronic otitis media (19). Although the nomenclature has changed several times since its original description, including the term *Alcaligenes xylosoxidans*, biochemical and molecular studies have now reclassified it as "*Achromobacter xylosoxidans*" (20). Of the two currently recognized subspecies, *A xylosoxidans* subspecies *xylosoxidans* and *A xylosoxidans* subspecies *denitrificans*, the former is considered to be more relevant in clinical disease (11). In light of recent taxonomic changes, we elected to categorize all previous cases of *Alcaligenes xylosoxidans* and all organisms not identified at the subspecies level as "*Achromobacter xylosoxidans*", for the purpose of the present review. *A xylosoxidans* has low virulence but can cause significant disease in hosts with impaired immunity, chronic illnesses or prosthetic devices (2,21,22). Two unnamed species closely related to *A xylosoxidans*, "*Achromobacter* groups B and E" and *Achromobacter* F, have also been recovered from human blood isolates (23,24). We reviewed nine cases of endocarditis secondary to *A xylosoxidans*, one case secondary to *Achromobacter* group B, and two cases secondary to an unidentified *Achromobacter* species.

A xylosoxidans is a causative pathogen in abdominal infections, pneumonia, meningitis, urinary tract infections, osteomyelitis and ocular infections (25-30). It has also been implicated in hospital outbreaks and has been isolated from faucets, contaminated chlorhexidine solutions, disinfectant dispensers and intravenous contrast dye (22,31-34). Bacteremia secondary to *A xylosoxidans* is uncommon, and the majority

of cases are nosocomial (2,3,31). Endocarditis secondary to *Achromobacter* species is rare, with only 13 cases reported in the English literature including the present one.

A xylosoxidans infections are traditionally associated with immunocompromised or chronically ill populations (1,3,4,21,31,35). In our review of other case reports, one patient had undergone a hematopoietic stem cell transplant (12), and four other patients had chronic underlying illnesses including diabetes, heart failure or dialysis-dependent renal failure (7,8,11,13). One patient was an intravenous drug user (9). Eight of the 13 patients (62%), including our patient, had prosthetic valves or underwent septal patch repairs (8-10,14-17). In patients without immunodeficiencies or chronic illnesses, these mechanical disruptions in the host defense system could be an important risk factor for *Achromobacter* endocarditis.

Clinical manifestations of *Achromobacter* endocarditis varied, but all patients presented with fever (7-17). Polymicrobial endocarditis occurred in one patient (8%) and involved *Candida* species and *A xylosoxidans* (12). This incidence of coinfections is similar to that reported in *A xylosoxidans* bacteremia (2). Embolic complications associated with *Achromobacter* endocarditis were not uncommon, and occurred in five patients, including the present one (38%). One patient experienced a retinal hemorrhage (14), and another patient died after a cerebral embolus (15). One patient with an infected right atrial thrombus due to both *Candida* species and *A xylosoxidans* developed a pulmonary embolism and infiltrates (12). A fourth patient with mitral and aortic valve *A xylosoxidans* endocarditis experienced recurrent bacteremia associated with the liver, spleen, and renal infarcts and abscesses observed through imaging (8). Our patient had radiological evidence of splenic infarcts and a pulmonary embolus, although no confirmatory cultures were obtained from these sites. With the exception of the present case, no patient with embolic phenomena survived.

The crude mortality rate for patients with *A xylosoxidans* endocarditis is high. More than 50% of the patients with *A xylosoxidans* endocarditis died (7-8,12-16). Five of the surviving patients, including our patient, required surgical resection of the infected tissue in addition to a prolonged course of antibiotics (9-11,16). Only one patient with prosthetic heart tissue treated exclusively with antibiotics survived (17). Despite a full six-week course of appropriate antibiotic therapy with documented negative blood cultures, our patient developed recurrent *A xylosoxidans* subspecies *denitrificans* bacteremia on cessation of the antimicrobials. Complete resolution of the endocarditis required surgical resection of the diseased prosthetic valve with a repeat course of antibiotics.

Antibiotic susceptibility patterns for *A xylosoxidans* are characterized by resistance to the aminoglycosides, narrow-spectrum penicillins, first- and second-generation cephalosporins, some third-generation cephalosporins (cefotaxime and ceftriaxone) and aztreonam (2,35). *A xylosoxidans* is generally susceptible to ceftazidime, extended-spectrum penicillins, carbapenems and sulfonamides, while susceptibility to quinolones is variable (2). Susceptibility only to colistin was recently reported in a patient treated for an intra-abdominal abscess (25). Despite a high level of resistance to aminoglycosides, in vitro studies (2) suggest that the use of gentamicin with trimethoprim/sulfamethoxazole or beta-lactams may be synergistic. The *A xylosoxidans* subspecies *denitrificans* antibiotic susceptibility pattern in our patient was similar to those previously reported in the literature (2,35), although there was some variability in aminoglycoside and cefepime susceptibilities between hospital #1 and our facility. This variance may be secondary to differences in antibiotic susceptibility testing between the two hospitals or from both isolates being near the minimum inhibitory concentration breakpoint for these antibiotics.

Ten patients (77%), including the present one, had sufficient data available to determine a health care-associated relationship with the infection (7-9,12,14-17). Nosocomial infective endocarditis is defined as developing within 72 h after hospital admission or within eight weeks of an invasive procedure (36). Some authorities advocate a six-month follow-up period for the surveillance of hospital-acquired infective endocarditis (37,38). Using this modified definition, all 10 cases of *Achromobacter* endocarditis were hospital acquired: three patients had central venous catheters (7,8,12) and seven patients, including the present patient, underwent prosthetic valve or interventricular septal surgery within six months of their symptoms (9,14-17). Two of these patients shared the same ethylene oxide heart pump, and infection was attributed to inadequate sterilization practices (16). The remaining three cases had insufficient information to be categorized as hospital acquired. One patient underwent recent dental work (10) and one patient had been admitted to the hospital within the previous three months (11); however, further details, such as invasive procedures, were not provided.

SUMMARY

We presented a patient with complicated prosthetic valve endocarditis secondary to *Achromobacter xylosoxidans* subspecies *denitrificans* that developed four months after pulmonary valve replacement. *Achromobacter* species are an emerging cause of Gram-negative endocarditis. The majority of cases are nosocomial; patients with prosthetic devices or central venous catheters appear to be disproportionately affected. Management of *Achromobacter* endocarditis is challenging, often requiring a combination of surgery and broad-spectrum antimicrobials. Although our patient initially failed a full six-week course of systemic antibiotics, she subsequently recovered after surgical resection of the affected valve and a second course of systemic antibiotics. Our case adds to the expanding body of literature on *Achromobacter* species endovascular infections. To our knowledge, this is the first confirmed reported case of endocarditis involving *Achromobacter xylosoxidans* subspecies *denitrificans*.

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