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Native-valve endocarditis caused by *Achromobacter xylosoxidans*: a case report and review of literature

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ABSTRACT

Achromobacter xylosoxidans is a Gram-negative aerobic bacterium first described by Yabuuchi and Ohyama in 1971. *A. xylosoxidans* is frequently found in aquatic environments. Abdominal, urinary tract, ocular, pneumonia, meningitis, and osteomyelitis are the most common infections. Infective endocarditis is rare. As far as we know, until now, only 19 cases have been described, including this current report. We report the case of community-acquired native valve endocarditis caused by *A. xylosoxidans* in an elderly patient without a concomitant diagnosis of a malignancy or any known immunodeficiency. The patient presented with a 2-month history of fever, weight loss, and progressive dyspnea. On physical examination, mitral and aortic murmurs were present, along with Janeway's lesions, and a positive blood culture for *A. xylosoxidans*. The transesophageal echocardiogram showed vegetation in the aortic valve, which was consistent with the diagnosis of infective endocarditis.

Keywords

Achromobacter; Infective Endocarditis; Native-Valve Endocarditis.

CASE REPORT

An 86-year-old woman with heart failure due to ischemic heart disease, polymyalgia rheumatica, idiopathic pulmonary fibrosis, non-dialysis-dependent chronic kidney disease and panic disorder was brought to the emergency room with a 2-month history of persistent daily high-grade fever (38.5 °C) and progressive dyspnea. She had been previously hospitalized for 15 days because of fever and dyspnea accompanied by a cough and hyaline sputum, when the laboratory work-up revealed a positive blood culture for *Achromobacter xylosoxidans*. At that time, there was no evidence of vegetation on a transthoracic echocardiogram (TTE), no abnormality on the abdominal

ultrasound or on the chest and abdominal computed tomography (CT). Also, she had a normal urinalysis and a negative urine culture. HIV, hepatitis B and C serology, and antinuclear antibodies were negative. The patient received an 8-day course of intravenous trimethoprim-sulfamethoxazole according to the blood culture sensitivity tests, followed by a 6-day course of the same orally administered antibiotic. She was discharged without fever, but the dyspnea remained unchanged.

On the eighth day following the withdrawal of the antibiotic, the fever relapsed and the patient restarted empirical treatment with the same antibiotic. Despite

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this new regimen of antibiotic, she was readmitted with a high-grade fever, progressive worsening of dyspnea, and new skin lesions on the palms of her hands and soles of her feet. Over the previous 2 months, she had lost 5 kg (10% of her usual weight). She denied any previous diagnosis of malignancy, and any use of intravascular devices or immunosuppressive therapy. She was regularly using carvedilol, atorvastatin, and aspirin, besides the previously mentioned antibiotic when readmitted.

During the physical examination, she was pale, with tachycardia (pulse of 108 bpm), blood pressure of 98/60 mmHg and normal axillary temperature of 36.8 °C. A systolic and diastolic cardiac murmur in the aortic area, and a systolic murmur in the mitral area, were easily audible. Pulmonary auscultation detected Velcro-like crackles, which were consistent with pulmonary fibrosis. The abdominal examination was painless; the liver was palpable at the right rib cage; the spleen was not palpable; and there was no dullness on percussion over the Traube's space. Multiple non-tender erythematous violaceous papules and macules were present in the patient's palms, fingers, thumbs, and soles, which was consistent with Janeway's lesions (Figure 1). The patient had a total dental prosthesis and the oral cavity was free of lesions. Upon readmission, trimethoprim-sulfamethoxazole was withdrawn and three sets of blood cultures were sampled at different puncture sites at 12-hour intervals.

The initial laboratory work-up showed an elevated C-reactive protein level of 120 mg/L (reference value [RV]: <5 mg/L) and an erythrocyte sedimentation rate at 170 mm/h (RV: <20 mm/h), normocytic and

normochromic anemia, thrombocytosis, a positive rheumatoid factor of 60 UI/mL (RV: <16 UI/mL) and a serum creatinine of 1.59 mg/dL (RV: 0.4-1.3 mg/dL), which was similar to the patient's previous creatinine determination; normal complement levels (C3 and C4) and a positive qualitative cryoglobulin's test. Urinalysis showed microscopic hematuria without erythrocyte dysmorphism and mild proteinuria. All blood culture sets were negative. A TTE was performed on the second day following readmission, which did not show any valvular vegetation. However, a left ventricular systolic dysfunction and aortic and mitral regurgitation were found.

During the first 2 days of hospitalization, the patient remained afebrile, but on the third and fourth day she presented an ongoing axillary temperature of 38.3 °C. Treatment with piperacillin-tazobactam was scheduled for a 6-week regimen. Another thoracic and abdominal CT was performed, ruling out any suspected site of infection or malignancies. A transesophageal echocardiography (TEE) showed a 4 mm vegetation on the non-coronary cusp of the aortic valve.

During hospitalization, the patient presented worsening signs of heart failure, including weight gain, sacral and lower limbs pitting edema, bilateral rales crackles, and hepatojugular reflux, which improved with diuretics and vasodilators titration. Furthermore, she presented five episodes of supraventricular tachycardia, which was treated with amiodarone. She completed a 6-week course of piperacillin-tazobactam along with improved clinical and laboratorial status. Her fever subsided after the 15th day of antibiotic treatment; the arrhythmia remained controlled and the heart failure became asymptomatic. She was discharged after 55 days of hospitalization for an outpatient clinical follow-up.

A signed informed consent for publication was obtained, and the manuscript is in accordance with the institution's ethics committee.

DISCUSSION

Achromobacter xylosoxidans is a Gram-negative aerobic bacterium first described by Yabuuchi and Ohya in 1971 in patients with chronic purulent otitis media.¹ *A. xylosoxidans* is frequently found in aquatic environments² and infections are frequently



Figure 1. Janeway's lesions in the patient's hand.

associated with cardiovascular disease, malignancy, and immunosuppression,^{3,4} and are mostly a nosocomial infection.³ Pneumonia, meningitis, osteomyelitis, plus urinary tract, abdominal, and ocular are the most usual infections, while native valve endocarditis is rarely reported.²

Searching in the PubMed, Scielo, Lilacs, Scopus, and Web of Knowledge using the keywords "*Achromobacter xylosoxidans*" and "infective endocarditis" (IE) we were able to retrieve only 18 cases of *A. xylosoxidans* endocarditis in the English

language (Table 1). In our review, including our case, 6 of 19 (32%) patients were 60 years old or older; 3/19 (16%) were intravenous drug users; 3/19 (16%) had intravenous devices; 8/19 (42%) had prosthetic valve involvement. Considering the treatment and the outcome: 11 of 19 (58%) required surgical intervention; 8/17 (47%) died, 2 of the 8 (22%) were from the operated group and the other 6 (75%) were from the clinically treated group.

IE presents an incidence of 3.6/100,000 population/year,²² and its diagnosis remains challenging since new

Table 1. Reported cases of *Achromobacter xylosoxidans* IE

Author	Age (y/m)	Risk Factor for IE	Comorbidities	Valve	Prosthetic	Antibiotic	Surgery	Died
This Case	86 y	None	IHD, pulm. fibrosis, CKD, Polymyalgia	Ao	No	TMP-SMX + Piperacillin-tazobactam	No	No
Kumar et al. ⁵	54 y	NA	CKD, CRF, H	M + Ao	No	Vancomycin + Piperacillin-tazobactam + Gentamicin	Yes	NA
Bhattarai et al. ⁶	37 y	IDU + PV	NA	Mitral	Yes	Meropenem	Yes	No
Levo et al. ⁷	6 m	IVC + calcified MV	arterial calcification	M	No	Piperacillin-tazobactam + Meropenem + Levofloxacin + TMP-SMX+ Colistin	No	No
Rafael et al. ⁸	50 y	CS	VSDR	P + RVOT	No	NA	Yes	No
Sawant et al. ⁹	62 y	PV+ PM	AF, CHF, COPD, CKD	M + Ao + PM	Yes/No/-	Piperacillin-tazobactam + meropenem + TMP-SMX+ Rifampin + Amikacin	Yes	No
Tokuyasu et al. ¹⁰	86 y	PV	NA	Ao	Yes	Carbapenem	No	Yes
Derber et al. ²	54 y	PV+ Fallot's T	Fallot's T	P	Yes	Piperacillin-tazobactam + Imipenem-cilastatin + Levofloxacin	Yes	No
Store et al. ¹¹	79 y	None	H, AF, TIA	M + Ao	No	Meropenem	No	Yes
Malek-Marín et al. ¹²	50 y	Catheter	CKD	NA	-	NA	Yes	Yes
Ahmed et al. ¹³	69 y	PV	DM, H, CKD CABG	M + Ao	No/Yes	Etrapenum + Tigecycline + TMP-SMX	Yes	Yes
Van Hal et al. ¹⁴	37 y	PV+ IDU	NA	Ao	Yes	Meropenem	Yes	No
Yan et al. ¹⁵	35 y	IDU+ TR + MP	Hepatitis C	T	No	Piperacillin-tazobactam + Amikacin + Ceftazidime	Yes	NA
Nanuashvili et al. ¹⁶	46 y	None	DM, bullous emphysema, IS	M + Ao	No	Ampicillin-sulbactam + Cotrimoxazole	Yes	No
Ahn et al. ¹⁷	35 y	CS+ PM	VSDR, CHB with PM	PM + RVOT	-	Ceftazidime + Piperacillin	Yes	No
Martino et al. ¹⁸	33 y	IVC	bone marrow transplant	NA	-	Aztreonam + Amikacin	No	Yes
Davis et al. ¹⁹	30 y	NA	HF	NA	-	None	No	Yes
Olson et al. ²⁰	35 y	Aortic surgery + PV	NA	Ao	Yes	Carbenicillin + TMP-SMX+ Rifampin + moxalactam + azlocillin	No	Yes
Lofgren et al. ²¹	77 y	PV	Rheumatic dis. + PV	M + Ao	No/ Yes	Tobramycin + carbenicillin + TMP-SMX + moxalactam	No	Yes

AF: atrial fibrillation; Ao: Aortic; CABG: coronary artery bypass grafting; CHB: complete heart block; CHF: congestive heart failure; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CS: cardiac surgery; DM: diabetes mellitus; H: Hypertension; HF: heart failure; IDU: intravenous drug user; IHD: ischemic heart disease; IS: ischemic stroke; IVC: intravenous catheter; M: Mitral; NA: not available; P: Pulmonary; PM: Pacemaker; PV: prosthetic valve; RVOT: right ventricular outflow tract; T: Tricuspid; TIA: transient ischemic accident; TMP-SMX: trimethoprim-sulfamethoxazole; TR: tricuspid regurgitation; VSDR: ventricular septal defect repair.

etiologic agents have been increasingly reported. Similarly, the incidence of IE is increasing in the elderly population, which may present non-characteristic clinical symptoms, such as fatigue, malaise, and anorexia.²³ Major clinical societies recommend the use of the Modified Duke Criteria,²⁴ which is based on pathological and clinical findings.²⁵ Considering the case reported herein, the patient had a previous hospitalization with fever and dyspnea and, on the second hospitalization, presented four minor clinical Duke's criteria;²⁴ namely, (i) Janeway's lesions; (ii) positive rheumatoid factor; (iii) fever; and (iv) a positive blood culture on the previous hospitalization.

Therefore, the patient's condition was classified as a "possible IE." An initial TTE did not show any evidence of vegetation. However, as the patient had a high pre-test probability of IE, a TEE was performed, which evidenced cardiac vegetation on the aortic valve. The diagnosis of IE was made on the basis of the presence of four minor and one major clinical Modified Duke Criteria.²⁴ TTE identifies only 25% of vegetation <5 mm while TEE for all vegetation sensitivity ranges between 90% and 100%.²⁶⁻²⁸ Vegetation size is associated with the risk of embolism and vegetation >1 cm is a predictive value for mortality risk in patients over 60 years of age.^{29,30}

In 1986, the review made by Chandrasekar et al.,³¹ regarding *A. xylosoxidans* bacteremia, found resistance to aminoglycosides and a susceptibility to trimethoprim-sulfamethoxazole and beta-lactam antibiotics. Subsequently, two other reviews (by Duggan et al.⁴ in 1996 and Gómez-Cerezo et al.³ in 2003) found susceptibility to antipseudomonal penicillins and carbapenems, and resistance to aminoglycosides and second-generation cephalosporins. Duggan⁴ found that trimethoprim-sulfamethoxazole was bacteriostatic and Gómez-Cerezo³ found resistance to this antibiotic. Two recent case reports of infections due to *A. xylosoxidans* found additional susceptibility to amoxicillin-clavulanate.^{32,33} Due to the scarcity of the cases reported, there is no consensus on the best antimicrobial regimen for endocarditis caused by *A. xylosoxidans*. However, it seems that antipseudomonal penicillins and carbapenems are the best choice, based on bacteremia studies and case reports.^{2-7,9-11,13-16,31}

In our case report, the patient had a community-acquired, native-valve IE, which was attributed to this

pathogen. She also had cardiovascular disease, which is a risk factor for *A. xylosoxidans* infection, but the site involved (cardiac) is unusual for this bacteria. When the fever recurred, we started a piperacillin-tazobactam regimen based on the antibiogram and the available literature data. The patient had a favorable response to the antibiotic course and was discharged without any other symptoms.

IE in the elderly can have mild symptoms and diagnosis can be very challenging. This report emphasizes the necessity to investigate patients with long-lasting fever and validates positive blood cultures, even with uncommon bacterium. It also highlights that clinicians should consider the diagnosis of IE and the performance of a TTE when most of the common sites of infection were ruled out.

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