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Infective endocarditis due to Achromobacter xylosoxidans: A case report and a literature review

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Case Report

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ABSTRACT

Congenital heart disease (CHD) and invasive cardiac procedures are risk factors for infective endocarditis (IE) in children. IE with *Achromobacter xylosoxidans* is a rare case and has a high mortality rate. This case report and literature review aim to understand the risk factors, diagnosis, therapy, and outcome of IE wirh *Achromobacter xylosoxidans*. We observed a 14-months-old boy with ventricular septal defect (VSD), a history of cardiac catheterization, 9 days fever and febrile convulsion; and tachycardia and pansystolic murmur on the tricuspid valve were found. Transthoracic echocardiography revealed vegetation on the tricuspid valve. Monomicrobial clinical isolates of *Achromobacter xylosoxidans* were consistently found in three samples of aerobic blood culture bottles. The patient was treated with definitive antibiotic therapy with 200 mg/8 hours of ceftazidime for 21 days. Bacterial growth was not found in the blood culture evaluation which was performed after 48 hours of the therapy. Also, it was found that in the follow up period the patient had no fever on the sixth day, and the vegetation size was reduced. A patient with CHD, especially with VSD as an underlying condition who had a history of cardiac catheterization and accompanied by fever and heart murmur, should be suspected of having IE. Then the definitive antibiotic therapy with ceftazidime contributed to a better clinical outcome.

Penyakit jantung bawaan (PJB) dan riwayat tindakan invasif jantung merupakan faktor risiko endokarditis infektif (EI) pada anak-anak. Kasus Achromobacter xylosoxidans *EI sangat jarang dan memiliki risiko kematian tinggi. Laporan kasus dan tinjauan literatur ini bertujuan untuk memahami faktor risiko, diagnosis, terapi, dan luaran* Achromobacter xylosoxidans *EI. Kami melaporkan, anak laki-laki berusia 14 bulan dengan* ventricular septal defect *(VSD) dan riwayat kateterisasi jantung mengalami demam sejak 9 hari dan kejang demam, ditemukan takikardia dan murmur pansistolik pada katup trikuspid. Pemeriksaan transtorakal ekokardiografi didapatkan vegetasi pada katup trikuspid. Isolat klinis tunggal Achromobacter xylosoxidans secara konsisten ditemukan pada 3 sampel botol kultur darah aerob. Pasien diterapi dengan ceftazidime 200 mg/8 jam selama 21 hari. Tidak ditemukan pertumbuhan bakteri pada kultur darah evaluasi pada 48 jam setelah terapi ceftazidime. Pemantauan selanjutnya, pasien mengalami tidak demam pada hari ke-6 dan ukuran vegetasi berkurang. Pasien PJB VSD dengan riwayat kateterisasi jantung disertai demam dan murmur jantung sebaiknya dicurigai menderita EI. Pengobatan antibiotik definitif dengan ceftazidime memunculkan hasil klinis yang lebih baik.*

INTRODUCTION

Children with congenital heart disease (CHD), who have a history of invasive procedures such as cardiac catheterization or cardiac surgery, probably suffer infective endocarditis (IE) in the follow up period.[1,2] Some of microorganisms causing IE in children are Gram-positive cocci bacteria, including the group of *Streptococcus* (*Streptococcus viridans* and *Streptococcus hemolyticus*), *Staphylococcus* (*Staphylococcus aureus* and *coagulase-negative*) and *Enterococcus*. Meanwhile, the HACEK group (*Haemophilus* sp., *Aggregatibacter* sp., *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* sp.) is less common microorganisms causing IE.[1,3-5]

Achromobacter xylosoxidans is an opportunistic pathogen in an immunocompromised patient and rarely causes IE. However, the mortality rate of IE with *Achromobacter xylosoxidans* is considerably high, reaching 50% of cases.[6-10] We presented a case of IE with *Achromobacter xylosoxidans* in a child with ventricular septal defect (VSD) and a history of cardiac catheterization. In addition, we conducted a literature review regarding this case to understand the risk factors, diagnosis, therapy, and clinical outcome of *Achromobacter xylosoxidans* causing IE.

CASE DESCRIPTION

A 14-months-old boy was admitted with fever for nine days and febrile convulsion. He had a medical history of VSD and at the age of 7 months undergoing catheterization which revealed a large mal-alignment VSD with pulmonary hypertension. On physical examination, we found his temperature by 39°C, tachycardia and pansystolic murmur on the tricuspid valve. There was no skin lesion, Osler node, Janeway lesion nor splinter haemorrhage.

Blood examinations showed relative lymphocytosis and monocytosis with leucocyte count of $10.59x10^3/\mu L$, 75.4% lymphocytes and 11.6% monocytes. There were no increased levels in erythrocyte sedimentation rate nor C-reactive protein. The chest X-ray showed both the atrium and right ventricle hypertrophy with pulmonary hypertension. Transthoracic echocardiography (TTE) examination revealed vegetation on the tricuspid valve. Three sets of aerobic and anaerobic blood culture bottles (BACTEC, Becton, Dickinson and Co, Franklin Lakes, NJ) were obtained for microorganism identification and antibiotic susceptibility test (Vitek 2 System, BioMérieux Inc, USA). Monomicrobial clinical isolates of *Achromobacter xylosoxidans* were consistently found in three samples of aerobic blood culture bottles. The result of antibiotic susceptibility test indicated that these clinical isolates were susceptible to ceftazidime, cefepime, meropenem, piperacillin/tazobactam, tigecycline and trimethoprim/sulfamethoxazole, intermediate to ciprofloxacin, and resistant to gentamicin, amikacin, cefazolin, ceftriaxone and aztreonam.

Previously, the patient was empirically treated with 400 mg/6 hours of ampicillin/ and 40 mg/24 hours of gentamicin.. After the result of antibiotic susceptibility test was obtained, the therapy was switched to 200 mg/8 hours of ceftazidime for 21 days. The choice of the antibiotic therapy was also based on the recommendation of IE in children for nosocomial endocarditis associated with vascular cannula or prosthetic valve endocarditis less than one year, and ceftazidime was susceptible in 40% cases of IE with *Achromobacter xylosoxidans* and resulted in a good clinical outcome. During the follow up period, the second two sets of blood culture were performed in 48 hours after ceftazidime therapy, and there was no bacterial growth found. In further follow up, we found that the patient was free of fever on the sixth day after ceftazidime administration and that TTE evaluation pointed out reduced vegetation size.

DISCUSSION

Achromobacter xylosoxidans is a Gram-negative, aerobic rod, catalase and oxidase

positive, motile with peritrichous flagella and nonfermenting bacterium (Figure 1). *Achromobacter xylosoxidans* inhabits aqueous environments, including well water, while nosocomial outbreak are attributed to disinfectant solutions, intravenous fluids, saline solutions, and water in humidifiers.[10-13] *Achromobacter xylosoxidans* is an opportunistic human pathogen, which is capable of causing a variety of infections, particularly in immunocompromised hosts and patients with underlying chronic diseases.[6-9,11-16] The case observed is the first IE with *Achromobacter xylosoxidans* since 2015-2021 in Dr. Sardjito Hospital, Yogyakarta, Indonesia. The case observed is the first IE with *Achromobacter xylosoxidans* since 2015-2021 in Dr. Sardjito Hospital, Yogyakarta, Indonesia. The literature review of IE with *Achromobacter xylosoxidans* is based on Medline/PubMed database with the keywords "*Achromobacter xylosoxidans*" and "endocarditis" with filter of English and full text, and 9 cases from the literature search from 1981-2018 were obtained (Table 1).

This case was IE with *Achromobacter xylosoxidans*, and the VSD became its underlying condition and a history of cardiac catheterization was its risk factor. Congenital heart disease is one of risk factors for IE in children.[1,2,11,13,14] High velocity jets or low pressure side of a cardiac structural lesion contribute to aberrant flow, which can cause endothelial injury and allow either direct infection or the development of nonbacterial thrombotic endocarditis which is an uninfected platelet-fibrin thrombus. The thrombus serves as a site of bacterial attachment during transient bacteremia.[1,17,18] There were four cases of IE including this current case which occurred in native valves with CHD.[6,8,10] In addition, previous heart surgery, use of prosthetic heart patches or valves and insertion of invasive devices such as catheterization were common risk factors of postoperative or nosocomial for IE complication (60%).[7,9-11,13-15]

Fever was presented in 90% of IE cases, and 85% of cases had heart murmur suggestive to valvulitis.[2] Subacute vascular and immunologic manifestations of IE, such as Janeway lesion, Roth's spot, petechiae, splinter haemorrhage, Osler node and glomerulonephritis, are less common in children.[1] Increased CRP and ESR, leucocytosis and haematuria can strengthen the suspiciousness to IE although they are less specific. Increased CRP and ESR were found in 67% of cases which reflected inflammation, and leucocytosis was found in 20-50% of cases.[17,18] Then TTE was the main imaging modality for IE diagnosis. In this case, TTE examination showed vegetation on the tricuspid valve. The sensitivity of TTE for diagnosing vegetation on native valves is 70% while the specificity is about 90%.[1,2] In this case report, transoesophageal echocardiography (TOE) was not done in this patient. TOE should also be performed in patients with positive TTE to rule out local complications.[2,19]

Blood culture for microorganism identification and susceptibility testing are essential in an IE diagnosis. Specimen from vegetation resection or embolic fragment is the gold standard for diagnosing IE. However, modified Duke criteria, which consist of clinical symptoms, echocardiography and biological findings from blood culture and from serological examinations, can be used if the gold standard is not possible to obtain.[1,2,18] Three sets of aerobic and anaerobic peripheral blood cultures were obtained in this case and monomicrobial clinical isolates of *Achromobacter xylosoxidans* were consistently resulted in all three samples of aerobic blood culture bottles. Anaerobic bacteria rarely cause IE so that aerobic blood culture are usually more emphasized.[2] Blood sampling is obtained before antibiotic therapy is given, in any particular febrile phase, because bacteraemia in IE is continuous, constant at low degree and consistent. Blood sampling is drawn from peripheral vein rather than from the central venous catheter to avoid contamination, using a sterile technique, with blood volume drawn about 1-3 mL in infants and 5-7 mL in older children.[1,2]

This patient was treated with empirical antibiotics ampicillin and gentamicin. A combination of a β-lactam plus an aminoglycoside

Table 1. Characteristics of infective endocarditis cases with *Achromobacter xylosoxidans*

Case & reference number	Location	Age (years), sex	Underlying diseases	Predisposing factors	Signs and symptoms	Heart involved	Antibiotics therapy and Susceptible antibiotics	Heart surgery	Clinical outcome
This case	Yogyakarta, Indonesia	1, male	VSD	Cardiac catheterization	Fever, tachycardia	TV	AMP†*, GEN†* → CAZ*, FEP, MEPM, SXT, TGC, TZP	No	Survive
Xia, 2018[6]	Brooklyn, New York, USA	66, male	Hypertension, diabetes mellitus, chronic renal failure, colitis	Hemodialysis	Fever, diarrhea,nausea and vomiting, elevated Troponin I and BNP	MV	MEPM* → LVX*, SXT*, CIP, TZP	No	Death
Rafael, 2014[11]	Cleveland, Ohio	50, female	Intracardiac abscess, cutaneous fistula	VSD repair, history IE	Cutaneous fistula and sternal wound	VSD pledge	TZP*, SXT*	Debridement and removal VSD pledge	Survive
Tokuyasu, 2012[7]	Shimane, Japan	86, female	IE, sepsis	Prosthetic AV, Mycobacterium nontuberculous infection	Fever, cough, hypotension, relative neutrophilia, elevated CRP	Prosthetic AV	MEPM* → DOR†* → panipenem/ betamipron†*, IPM, MIN, CFP, PIP, CAZ	No	Death
Derber, 2011[13]	Richmond, Virginia, USA	54, female	IE	Tetralogy of Fallot with BT-shunt, PV replacement	Fever, tachycardia, hypotension, heart failure, abdominal pain, leucocytosis	Prosthetic PV, anterior mediastinum and pulmonary outflow tract abscess	TZP*, LVX* → imipenem/ cilastatin†*, LVX*, SAM, IPM, CAZ, CIP, SXT	Replacement prosthetic PV, debridement mediastinum anterior and pulmonary outflow tract abscess	Survive
Storey, 2010[8]	St Leonards-on-Sea, East Sussex, UK	79, female	Sepsis, IE, atrial fibrillation, transient ischemic attack, hypertension	Atrial fibrillation, transient ischemic attack, hypertension	Fever, lethargy, weight loss, delirium, cardiomegaly, pleural effusion, leucocytosis, absolute neutrophilia, elevated CRP and INR	MV and AV	SXT†*, MEPM*, TZB	No	Death

Case & reference number	Location	Age (years), sex	Underlying diseases	Predisposing factors	Signs and symptoms	Heart involved	Antibiotics therapy and Susceptible antibiotics	Heart surgery	Clinical outcome
Van Hal, 2008[15]	Darlinghurst, New South Wales, Australia	37, male	Multiple root aorta abscess, IE, prosthetic MV	History IE, prosthetic MV, intravenous drug user	Fever, hypotension, congestive heart failure	Root aorta, prosthetic MV	MEPM*	Replacement prosthetic AV and homograft root aorta	Survive
Ahn, 2004[14]	Dong-gu, Gwangju, Korea	35, male	VSD, complete heart block	VSD with patch closure, pacemaker implant, dental scaling and root planning	Fever, systolic murmur at PV, cardiomegaly, anaemia, leucocytosis, elevated ESR and CRP	Right ventricle endocardium, patch	CAZ*, PIP*, CFP, IPM, SXT	Removal of infected wires, infected Dacron patch, vegetation resection and RV wall curettage	Survive
Martino, 1990[9]	Rome, Italy	33, male	IE, myelofibrosis	Central venous catheter	Fever, hypotension, pancytopenia, pulmonary emboli	Right atrium thrombus, secondary pulmonary emboli	ATM*, AMK*	No	Death
Lofgren, 1981[10]	Minneapolis and St Paul, Minnesota, USA	77, female	Rheumatic heart disease, aorta stenosis, mitral regurgitation	Prosthetic AV	Fever, systolic murmur, right retina haemorrhage	MV and AV	SXT*	No	Death

†: empirical antibiotic used, *: susceptible antibiotic used

IE: infective endocarditis, VSD: ventricular septal defect, AV: aortic valve, MV: mitral valve, PV: pulmonal valve, TV: tricuspid valve, BT-shunt: Blalock-Taussig shunt, BNP: brain natriuretic peptide, CRP: C-reactive protein, AMK: amikacin, AMP: ampicillin, ATM: aztreonam, CAZ: ceftazidime, CFP: cefoperazone, CIP: ciprofloxacin, DOR: doripenem, FEP: cefepime, GEN: gentamicin, IPM: imipenem, LVX: levofloxacin, MEPM: meropenem, MIN: minocycline, PIP: piperacillin, SAM: ampicillin/sulbactam, SXT: trimethoprim/sulfamethoxazole, TGC: tigecycline, TZB: tazobactam, TZP: piperacillin/tazobactam.

antibiotic (such as ampicillin/sulbactam or amoxicillin/clavulanate plus gentamicin, with/without vancomycin) or vancomycin plus gentamicin can be given for community-acquired native valves or late prosthetic valve (≥12 months post-surgery) endocarditis.[1,2,18] However, in this case the patient had undergone catheterization for 7 months previously, so nosocomial endocarditis associated with vascular cannula should be considered, which could be treated empirically with vancomycin plus gentamicin plus cefepime or ceftazidime.[1]

Once the pathogen is identified, the antibiotic therapy must be adapted to its antimicrobial susceptibility test result. The empirical antibiotic therapy was then switched to 200 mg/8 hours of ceftazidime for 21 days according to the antibiotic susceptibility test result. Antibiotic susceptibility test for IE with *Achromobacter xylosoxidans* in this case was compared to previous studies (Table 1). It showed that trimethoprim/sulfamethoxazole was still sensitive in 70% of cases (i.e. in this case and reference no. 6,8,10,11,13,14); meropenem was sensitive in 50% (i.e. in this case and reference no. 6-8,15); piperacillin/tazobactam was sensitive in 40% (i.e. this case and reference no. 3,11,13); ceftazidime was sensitive in 40% (i.e. in this case and reference no. 4,13,14); while cefepime and tigecycline were only sensitive in this case. The definitive antibiotic therapy, 200 mg/8 hour of ceftazidime, was administered for 21 days according to the antibiotic susceptibility test. Meropenem, cefepime and tigecycline were classified into restricted antibiotic as part of antibiotic stewardship efforts at Dr. Sardjito Hospital, so those were less chosen than ceftazidime and trimethoprim/sulfamethoxazole which were classified into watch antibiotic. The antibiotic trimethoprim/sulfamethoxazole was still sensitive in 70% of cases (i.e., in this case and reference no. 6,8,10,11,13,14), but 3 of 4 patients who used trimethoprim/sulfamethoxazole as empirical antibiotic revealed unfavourable outcomes (i.e., reference no. 6,8,10). The antibiotic ceftazidime used was also in line with the American Heart Association statement of empirical antibiotic recommendation for nosocomial endocarditis associated with vascular cannula or prosthetic valve endocarditis less than 1 year.[1] In addition, the case report of ceftazidime used with vegetation resection in postoperative VSD cases and pacemaker insertion in complete heart block also provided good outcomes.[11]

CONCLUSION

We presented a rare case of IE due to *Achromobacter xylosoxidans* with clinical signs of fever and heart murmur which had VSD as an underlying condition and underwent cardiac catheterization previously. This case showed good clinical outcomes under antibiotic therapy of ceftazidime.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests, and informed consent was obtained from the patient.

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