รายงานผู้ป่วย Case Report

การติดเชื้อ *Achromobacter xylosoxidans* ในกระแสเลือดในผู้ป่วยวัณโรคดื้อยาสเตรปโตมัยซิน : รายงานผู้ป่วย

Achromobacter xylosoxidans bacteremia in a patient with streptomycin-resistant tuberculosis: A case report

ทศพร เจริญจิต
โรงพยาบาลแก้งคร้อ ชัยภูมิ

Dhosaporn Charoenjit
Kaeng Khro hospital, Chaiyaphum

DOI: 10.14456/dcj.2021.95
Received: October 20, 2020 | **Revised:** December 30, 2020 | **Accepted:** December 31, 2020

บทคัดย่อ

บทนำ *Achromobacter xylosoxidans* เป็นเชื้อที่พบได้ในสิ่งแวดล้อมทั้งของชุมชนและโรงพยาบาล มักก่อโรคในผู้ป่วยภูมิคุ้มกันบกพร่อง มีความสามารถในการดื้อยาสูง การรักษาจึงขึ้นกับแบบแผนความไวต่อยาปฏิชีวนะที่พบในเชื้อของผู้ป่วยแต่ละราย ในเดือนสิงหาคม พ.ศ. 2563 โรงพยาบาลแก้งคร้อพบผู้ป่วยติดเชื้อ *Achromobacter xylosoxidans* ในกระแสเลือด 1 ราย เป็นผู้ป่วยเพศชาย อายุ 50 ปีอาชีพทำนา สูบบุหรี่ 20 ซอง-ปี มีไข้หนาวสั่น 3 วัน หอบเหนื่อยมาห้องฉุกเฉินโรงพยาบาลแก้งคร้อ ประวัติอดีตเคยป่วยด้วยวัณโรคปอดเสมหะบวกครั้งแรกใน พ.ศ. 2560 รักษาครบตามกำหนด แต่วัณโรคปอดกลับเป็นซ้ำในเดือนพฤศจิกายน พ.ศ. 2561 ผู้ป่วยกินยารักษาวัณโรค 6 สัปดาห์แล้วขาดการรักษา ผลเพาะเชื้อวัณโรคจากเสมหะพบการดื้อยาสเตรปโตมัยซิน การเจ็บป่วยในครั้งนี้ผู้ป่วยมีภาวะทางเดินหายใจล้มเหลวและติดเชื้อในกระแสเลือดจึงได้รับการใส่ท่อช่วยหายใจและยาปฏิชีวนะเซฟตาซิดิมทางหลอดเลือด ผลเพาะเลี้ยงแบคทีเรียจากเลือดขึ้นเชื้อ *A. xylosoxidans* ผลการรักษาผู้ป่วยเสียชีวิตจากภาวะทางเดินหายใจล้มเหลว สรุป การติดเชื้อวัณโรคปอดไม่มีหลักฐานว่าเพิ่มความเสี่ยงต่อการติดเชื้อ *A. xylosoxidans* แต่การที่ผู้ป่วยมีภาวะหลอดลมโป่งพองจากการรักษาวัณโรคไม่เหมาะสมและมีแผลเป็นในปอดอาจเพิ่มความเสี่ยงในการติดเชื้อที่ปอดและนำไปสู่การติดเชื้อในกระแสเลือดได้ การติดเชื้อ *A. xylosoxidans* แม้จะพบน้อย แต่อัตราการเสียชีวิตของผู้ป่วยสูง ในผู้ป่วยภูมิคุ้มกันบกพร่องที่มาด้วยการติดเชื้อควรตระหนักถึงเชื้อชนิดนี้ในการวินิจฉัยแยกโรคด้วย

ติดต่อผู้นิพนธ์ : ทศพร เจริญจิต อีเมล : drdhosaporn@gmail.com

Abstract

Introduction *Achromobacter xylosoxidans* can be found in both community and hospital environments. It can cause infection in immunocompromised patients and has many intrinsic characteristics that increase its likelihood of acquiring antibiotic resistance. Consensus guidelines on *A. xylosoxidans* treatment still remains a challenge; therefore, antibiotic choice must be considered by physician according to individual drug susceptibility patterns. In August 2020, the reported case, 50-year-old Thai male farmer presented to the

emergency room of Kaeng Khro Hospital in Chaiyaphum, Thailand, after experiencing fever with dyspnea for 3 days. He was a smoker (20 pack-years). He had a history of smear-positive pulmonary tuberculosis first diagnosed in 2017 with treatment completed. He had experienced a relapse of pulmonary tuberculosis in November 2018. Mycobacterium tuberculosis grew from sputum culture revealed its resistance to streptomycin. He had been lost to follow-up after 6 weeks of treatment. During this hospital course, he was diagnosed with acute respiratory failure and sepsis, and received endotracheal intubation and intravenous ceftazidime. Blood culture grew *A. xylosoxidans* with its antibiotic susceptibility pattern showing resistance to gentamicin, cefotaxime and ceftriaxone, and intermediate resistance to netilmicin. Despite treatment, he died due to respiratory failure. Conclusion there is no evidence showing that pulmonary tuberculosis increase the risk of *A. xylosoxidans* infection, but bronchiectasis from inadequate tuberculsosis treatment and pulmonary scarring possibly increase the risk of the opportunistic infection in lung and blood stream. Although *A. xylosoxidans* infection is rare, it is clinically important because of its high mortality rate. In immunocompromised individuals presenting with infection, we should include *A. xylosoxidans* infection in the differential diagnosis.

Correspondence: Dhosaporn Charoenjit E-mail: drdhosaporn@gmail.com

คำสำคัญ
ภาษาไทย อะโครโมแบคเตอร์ ไซโลโซซิแดนส์, ติดเชื้อในกระแสเลือด, อำเภอแก้งคร้อ, วัณโรคดื้อยาสเตรปโตมัยซิน

Keywords
Achromobacter xylosoxidans, bacteremia, Kaeng Khro, Streptomycin-resistant tuberculosis

Introduction

Achromobacter xylosoxidans is a non-fermentative gram-negative bacillus bacterium first described in 1971 by Yabuuchi and Oyama[1], based on seven chronic otitis media cases. *A. xylosoxidans* is particularly pathogenic in the immunocompromised hosts such as those affected by either solid[2] or hematologic[3] malignancy, chronic renal failure[4], or cystic fibrosis (CF)[5]. *A. xylosoxidans* is reported to cause bacteremia[6-8], pneumonia, cellulitis[9], pyelonephritis[10], ocular infections[11], osteomyelitis[12] and endocarditis[13]. The estimated prevalence of *A. xylosoxidans* infection is approximately 6% in cystic fibrosis patients of all age groups[14]. Thus far, there has been no reports about *A. xylosoxidans* prevalence in other populations. *A. xylosoxidans* infection is rare but is clinically important because of high mortality rate. *A. xylosoxidans* bacteremia has an 80% mortality rate in neonates and a 30% mortality rate in adults. The mortality rate is 65% in patients with meningitis and pneumonia[6], and over 50% in patients with endocarditis. Treatment of endocarditis requires both surgery and a 6-week course of antibiotics, and has been reported to recur even after a full course of antibiotics[13].

A. xylosoxidans bacteremia has been reported in an Indian female patient with sputum smear-positive pulmonary tuberculosis and diabetes[15]. However, to the best of the author's knowledge, there has been no previous case report of *A. xylosoxidans* infection

associated with pulmonary tuberculosis in Thailand.

Case report

A 50-year-old Thai man with a history of smoking 1-2 packs of cigarettes per day for 20 years presented at Kaeng Khro hospital. The patient was a farmer and lived in Chong Sam Mo sub-district, part of Kaeng Khro district. On August 3, 2020, the patient was admitted to the emergency room of the Kaeng Khro hospital due to fever with dyspnea for 3 days before admission. On admission, his weight was 42 kg, height was 170 cm, and body mass index (BMI) was 14.53 kg/m^2. His body temperature, blood pressure, and respiratory rate, pulse rate, and oxygen saturation at room air were at 37.5°C, 100/60 mmHg, 36 breaths/min, 116 beats/min, and 94% with accessory muscle use, respectively. Physical examination revealed the loss of temporal fat pad and decreased breath sound in the left lung with fine crepitation in both lungs. The patient was diagnosed as community-acquired pneumonia with acute respiratory failure. He received endotracheal intubation and intravenous ceftazidime before being referred to another hospital. When he admitted in Chaiyaphum hospital he developed septic shock. He recieved intravenous ceftriaxone, intravenous normal saline solution and intravenous norepinephrine due to low blood pressure. The patient was admitted to that hospital for 1 day, then he refused treatment and was subsequently discharged against medical advice. He along with his relatives signed an informed consent. After the patient discharged, Tuberculosis clinic (TBC) of Chaiyaphum hospital called TBC of Kaeng Khro hospital for following up the patient. But he died of respiratory failure after a few days from dischaged.

The history of his pulmonary tuberculosis diagnosis and treatment are showed in table 1. His first episode of pulmonary tuberculosis was diagnosed in June, 2017. While the relapse occurred in November, 2018. In these 2 episodes he presented with the same symptom which was hemoptysis.

Table 1. History of patient's previous pulmonary tuberculosis treatment

Date visited	June 2017	November 2018
Chief complaint	Hemoptysis for one month	Hemoptysis for one week
Present illness	-Weight loss from 50 kg to 45 kg -Low-grade fever	Weight loss from 47 kg to 42 kg
Investigations	-AFB: positive -Anti-HIV: non-reactive	-AFB: positive -Sputum molecular test for tuberculosis: susceptible to I and R -Sputum culture for tuberculosis: susceptible to I, R, and E, resistant to S
Diagnosis	Pulmonary tuberculosis, smear positive	Relapse pulmonary tuberculosis, smear positive with streptomycin-resistant
Management	2HRZE/10HE due to R induced jaundice	2SHE while awaiting tuberculosis culture result
Treatment outcome	-Bodyweight increased to 47 kg -Sputum AFB negative	The patient was lost to followup after 6 weeks of treatment due to relocating for work to another province

H=Isoniazid, R=Rifampicin, E= Ethambutol, Z=Pyrazinamide, S=Streptomycin, AFB=Sputum acid-fast bacillus

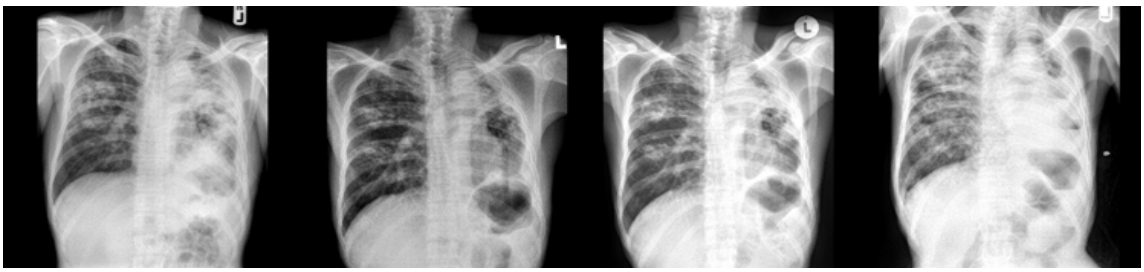

Figure 1. Patient's chest radiography images

From left to right: (a) 14/6/2017 before the first tuberculosis treatment; (b) 19/7/2018 after receiving a complete course of the first pulmonary tuberculosis treatment; (c) 1/11/2018 diagnosis of pulmonary tuberculosis relapse; (d) 3/8/2020 at the time of admission to the Kaeng Khro hospital.

Investigations: This was done in Kaeng Khro hospital before patient sent to Chaiyaphum hospital. Complete blood count revealed 7,930 cells/mm^3 white blood cells, composing of neutrophils (79%), lymphocytes (12%) and monocytes (9%). The patient's hemoglobin level, hematocrit, and platelet count were at 9.5 g/dL, 30%, and 300,000 per microliter of blood, respectively. Hemoculture grew *A. xylosoxidans*. Both bacterial isolation and antibiotic susceptibility tests were performed by MALDI Biotyper on the patient's blood. The sputum specimen quantity was inadequate for either bacteria or tuberculosis culture. His sputum was tested positive by acid-fast bacillus (AFB) stain. Anti-HIV antibody test was not performed. Chest radiography showed mediastinal shift to the left, along with cavitation and diffused consolidation in all lobes of the right lung. The left lung had a loss of volume due to traction bronchiectasis and multiple loculated lesions with air fluid levels.

Table 2. Antibiotic susceptibility pattern of *Achromobacter xylosoxidans*, based on the European Committee on Antimicrobial Susceptibility Testing guidelines

Antibiotic type	Minimal inhibitory concentration (MIC)	Results
Amikacin	16	S
Cefipime	8	S
Cefotaxime	>32	R
Ceftazidime	4	S
Cetriaxone	>32	R
Ciprofloxacin	1	S
Gentamicin	>8	R
Imipenem	1	S
Levofloxacin	1	S
Meropenem	≤0.5	S
Netilmycin	16	I
Piperacillin/tazobactam	≤8	S
Trimethoprim/sulfamethoxazole	≤1	S

S=susceptible, R=resistant, I=intermediate

Discussion

Achromobacter xylosoxidans can be found in both community[16] and hospital environments, sometimes causing disease outbreaks[4]. *A. xylosoxidans* has features, such as peritrichous flagella; it invades the host cells or cell membrane component and triggers the host immune response. Its capacity to survive in the human body is associated with its high iron-binding capacity and phosphate transport[17].

There are currently no consensus guidelines on the treatment of *A. xylosoxidans* infection, as this pathogen, even when acquired from a community source, has a high risk of antibiotic resistance[16]. There are five groups of genes that code efflux pumps in *A. xylosoxidans*[18]: major facilitator superfamily, multidrug and toxin extrusion, small multidrug resistance, ATP-binding cassette, and resistance-nodulation-division genes. Estimated efflux pump genes in *A. xylosoxidans* is between 40-50, for example, AxyXY-OprZ[19] for aminoglycosides excretion. MacA and macB[20] are genes specific for macrolide excretion. It can produce both penicillin-binding protein2 and beta-lactamase, thus becoming resistant to both penicillin and cephalosporin. Given these characteristics, the choice of an antibiotic and treatment duration should be determined based on each patient's drug susceptibility pattern and the exact location of the site of infection. In the previous case report of pulmonary tuberculosis and *A. xylosoxidans* pneumonia, the patient received intravenous piperacillin-tazobactum for two weeks and recovered[15]. This reported case received intravenous ceftazidime for empirical treatment of community-acquired pneumonia and died, despite the fact that *A. xylosoxidans* detected from blood culture was susceptible to ceftazidime.

The patient was most likely acquired *A. xylosoxidans* from some community source, as he was a farmer with no known history of hospital admission in the previous 2 years. His health status was poor due to his extensive smoking history, although there is no evidence to suggest that smoking increase the risk of *A. xylosoxidans* infection. In addition, the patient presented with characteristics consistent with those of cachexia, including loss of temporal fat pad and low BMI, suggesting malnutrition. He had previously been diagnosed with streptomycin-resistant pulmonary tuberculosis, for which he received inadequate treatment. Therefore his tuberculosis might have developed further drug resistance[21]. The drug sensitivity profile could not be determined due to insufficient collection of sputum for Mycobacterium tuberculosis culture. His chest radiography showed pulmonary parenchyma resembled that of bronchiectasis patients; therefore, *A. xylosoxidans* was suspected from pulmonary source. There is no evidence that pulmonary tuberculosis increases the risk of *A. xylosoxidans* infection, but bronchiectasis as a result of inadequate tuberculosis treatment and pulmonary scarring might lead to infection by the same mechanism as in CF. In addition, patients with drug-resistant tuberculosis, as in this reported case, have a lower treatment success rate and a higher mortality compared with patients with drug-susceptible tuberculosis[22]. Even though our patient was not at old-age or neutropenic, which are risk factors for mortality, he died of respiratory failure due to his poor lung condition. The antibiotic susceptibility pattern of *A. xylosoxidans* detected in this patient differed from those reported in previous studies[9, 18], and was resistant to fewer antibiotic types than previously reported cases[5, 20]. A whole genome sequence study revealed that most *A. xylosoxidans*

infections are resistant to a broad range of antibiotics including aminoglycosides, cephalosporins, and penicillin[23]. The whole genome sequencing on the *A. xylosoxidans* isolated from this patient was not performed due to limitation of resources.

Conclusion

A. xylosoxidans can be pathogenic in immunocompromised hosts and tends to be resistant to antibiotics. In immunocompromised individuals presenting with infection, *A. xylosoxidans* should be considered in the differential diagnosis of the causative organism. There are no standard treatment guidelines, and the choice of antibiotics depends on the drug susceptibility pattern. Pulmonary tuberculosis does not directly increase the risk of *A. xylosoxidans* infection, but infection may occur as a result of bronchiectasis in patients with inadequate tuberculosis treatment and pulmonary scarring.

Author statements

Funding sources

This work received no specific grant from any funding agency.

Conflicts of interest

The author declares that there are no conflicts of interest.

Ethical approval

This study was approved by the Human ethics committee of Chaiyaphum provincial public health number 52/2563

References

1. Yabuuchi E, Ohyama A. *Achromobacter xylosoxidans* n. sp. from Human Ear Discharge. Jpn J Microbiol. 1971;15(5):477-81.
2. Enriquez M, Favini A, Curl K. Sustained *Achromobacter Xylosoxidans* Bacteremia in a Patient with Adenocarcinoma of the Colon. Med Forum. 2015;15(1):5-7.
3. Tugcu D, Turel O, Aydogan G, Akcay A, Salcioglu Z, Akici F, et al. Successful treatment of multiresistant *Achromobacter xylosoxidans* bacteremia in a child with acute myeloid leukemia. Ann Saudi Med. 2015;35(2):168-9.
4. Reverdy ME, Freney J, Fleurette J, Coulet M, Surgot M, Marmet D, et al. Nosocomial colonization and infection by *Achromobacter xylosoxidans*. J Clin Microbiol. 1984;19(2):140-3.
5. Pérez Barragn E, Sandino Péez J, Corbella L, Orellana MA, Fernndez-Ruiz M. Achromobacter xylosoxidans bacteremia: clinical and microbiological features in a 10-year case series. Rev Esp Quimioter. 2018;31(3):268-73.
6. Duggan JM, Goldstein SJ, Chenoweth CE, Kauffman CA, Bradley SF. *Achromobacter xylosoxidans* bacteremia: Report of four cases and review of the literature. Clin Infect Dis. 1996; 23(3):569-76.
7. Weitkamp JH, Tang YW, Haas DW, Midha NK, Crowe JE. Recurrent *Achromobacter xylosoxidans* bacteremia associated with persistent lymph node infection in a patient with hyper-immunoglobulin M syndrome. Clin Infect Dis. 2000; 31(5):1183-7.
8. Gómez-Cerezo J, Suárez I, R-os JJ, Peña P, García de Miguel MJ, de José M, et al. *Achromobacter xylosoxidans* bacteremia: a 10-year analysis of 54 cases. Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol. 2003;22 (6):360-3.

9. Benjamin M. Davis, Glen F. Rall MJS. *Achromobacter xylosoxidans* bacteremia and cellulitis: a report of a case. Pediatr Dermatol. 2015;32(4):e186-7.
10. Tena D, González-Praetorius A, Pérez-Balsalobre M, Sancho O, Bisquert J. Urinary tract infection due to *Achromobacter xylosoxidans:* report of 9 cases. Scand J Infect Dis. 2008;40(2):84-7.
11. Reddy AK, Garg P, Shah V, Gopinathan U. Clinical, microbiological profile and treatment outcome of ocular infections caused by *Achromobacter xylosoxidans.* Cornea. 2009;28(10):1100-3.
12. Ozer K, Kankaya Y, Baris R, Bektas CI, Kocer U. Calcaneal osteomyelitis due to *Achromobacter xylosoxidans*: a case report. J Infect Chemother Off J Japan Soc Chemother. 2012;18(6):915-8.
13. Derber C, Elam K, Forbes BA, Bearman G. Achromobacter species endocarditis: A case report and literature review. Can J Infect Dis Med Microbiol. 2011;22(3):17-20.
14. Salsgiver EL, Fink AK, Knapp EA, LiPuma JJ, Olivier KN, Marshall BC, et al. Changing epidemiology of the respiratory bacteriology of patients with cystic fibrosis. Chest. 2016;149(2):390-400.
15. Chauhan K, Pandey A, Srivastava S, Gupta A. Pulmonary Infection Caused by *Achromobacter xylosoxidans* Report of Two Cases. J Clin Diagnostic Res. 2019;1-3.
16. Nakamot S, Sakamoto M, Sugimura K, Honmura Y, Yamamoto Y, Goda N, et al. Environmental distribution and drug susceptibility of *Achromobacter xylosoxidans* isolated from outdoor and indoor environments. Yonago Acta Med. 2017;60(1):67-70.
17. Swenson CE, Sadikot RT. Achromobacter respiratory infections. Ann Am Thorac Soc. 2015;12(2):252-8.
18. Hu Y, Zhu Y, Ma Y, Liu F, Lu N, Yang X, et al. Genomic insights into intrinsic and acquired drug resistance mechanisms in *Achromobacter xylosoxidans.* Antimicrob Agents Chemother. 2015;59(2):1152-61.
19. Bador J, Amoureux L, Blanc E, Neuwirth C. Innate aminoglycoside resistance of *Achromobacter xylosoxidans* is due to AxyXY-OprZ, an RND-type multidrug efflux pump. Antimicrob Agents Chemother. 2013;57(1):603-5.
20. Jakobsen TH, Hansen MA, Jensen PØ, Hansen L, Riber L, Cockburn A, et al. Complete Genome Sequence of the Cystic Fibrosis Pathogen *Achromobacter xylosoxidans* NH44784-1996 Complies with Important Pathogenic Phenotypes. PLoS One. 2013;8(7):8-11.
21. Faustini A, Hall AJ, Perucci CA. Risk factors for multidrug resistant tuberculosis in Europe: A systematic review. Thorax. 2006;61(2):158-63.
22. Ahmad N, Ahuja SD, Akkerman OW, Alffenaar J-WC, Anderson LF, Baghaei P, et al. Treatment correlates of successful outcomes in pulmonary multidrug-resistant tuberculosis: an individual patient data meta-analysis. Lancet. 2018;392(10150):821-34.
23. Choi H, Jinadatha C, Chatterjee P, Allton Y, Navarathna DH. Draft Genome Sequence of an Unusually Multidrug-Resistant Strain of *Achromobacter xylosoxidans* from a Blood Isolate . Microbiol Resour Announc. 2020;9(22):9-11.