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Original Article

Hospital-acquired pneumonia due to *Achromobacter xylosoxidans* in the elderly: A single-center retrospective study in Beijing

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Abstract

Introduction: *Achromobacter xylosoxidans* has been reported in several countries; however, hospital-acquired pneumonia (HAP) due to this organism in elderly patients in China remains rare.

Methodology: HAP due to *Achromobacter xylosoxidans* identified at the General Hospital of the People's Liberation Army in Beijing from January 2008 to October 2011 was studied. Detailed clinical manifestations were collected. To study the clinical risk factors for the imipenem-resistant strain, patients were divided into two groups: imipenem-resistant (21 cases) and imipenem-nonresistant (20 cases). Univariate and multivariate logistic regression were used.

Results: All patients were > 75 years of age, and 92.7% (38/41) were male. Nine patients died 30 days after infection. The mean acute physiology and chronic health evaluation (APACHE) II score and sequential organ failure assessment (SOFA) were 23.66 ± 7.71 and 6.93 ± 2.47, respectively. Almost all strains were resistant to aminoglycosides. However, the strains showed significant sensitivity to minocycline (MIN), piperacillin-tazobactam (PTZ), and cefoperazone-sulbactam (SCF). Compared with the imipenem-nonresistant group, more patients with imipenem-resistant infection had the following characteristics: use of an intubation, use of a proton-pump inhibitor (PPI), chronic obstructive pulmonary disease (COPD), and coronary artery disease (CHD). Among the four risk factors, COPD and CHD remained independent risk factors in the multivariate analysis.

Conclusions: HAP due to *Achromobacter xylosoxidans* occurred in severely ill elderly patients with a long-term indwelling catheter and many underlying diseases. Effective treatment of imipenem-resistant organisms is challenging. SCF, PTZ, and MIN may be useful for imipenem-resistant *Achromobacter xylosoxidans*.

Key words: *Achromobacter xylosoxidans*; hospital-acquired pneumonia; imipenem; elderly patients; resistance.

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Introduction

Achromobacter xylosoxidans has been reported in several countries. It is an oxidase-positive, catalase-positive, and highly motile non-fermenting Gram-negative bacterium that was first isolated from ear discharge and reported by Yabuuchi and Oyama [1]. This organism can be found in aquatic environments and soil. Moreover, due to its detection in many clinical specimens such as urine [2], blood [3-5], or cerebrospinalfluid [6-9], this organism has been gradually accepted as an opportunistic and emerging pathogenthat can lead to various nosocomial/non-nosocomial infections. Elderly patients who exhibit weakened immunity and malnutrition frequently have chronic infections and are frequently exposed to antibiotics, often resulting in the emergence of multidrug-resistant organisms.

Carbapenems, which are known as the last defensive line for the treatment of Gram-negative infections, are preferred for the treatment of multidrug-resistant Gram-negative strains. However, the overuse of carbapenems has resulted in the emergence of carbapenem-resistant organisms worldwide. Insertion of bla_{IMP} into plasmids in *Achromobacter xylosoxidan* has been described, potentially facilitating the spread of carbapenem-resistant strains [10].

Here, a retrospective study of 41 cases of HAP due to *Achromobacter xylosoxidans* was conducted, representing the largest number in China. The aim of this study was to illustrate the underlying diseases, the clinical manifestations, and outcome; to review the susceptibility of this organism to various antibiotics; and to discuss risk factors associated with imipenem resistance in patients with HAP due to *Achromobacter xylosoxidans*.

Methodology

Patients and clinical data

A retrospective review of HAP due to *A. xylosoxidans* was performed at the geriatric ward of the General Hospital of the People's Liberation Army (PLAGH) in Beijing from January 2008 to October 2011. HAP was diagnosed as previously described [11]. Clinical data included (1) basic demographics (sex, age); (2) underlying diseases; (3) time of positive culture; (4) invasive manipulation before onset (surgery, catheterization); (5) immunosuppressants; (6) chemotherapy; (7) antacids; (8) glucocorticoids; (9) use of antimicrobial drugs within 14 days before onset; (10) clinical features at onset (symptoms, blood routine tests, infectious indicators, and imaging, among others); (11) antimicrobial therapies; and (12) survival 30 days post-onset. The acute physiology and chronic health evaluation (APACHE) II score, sequential organ failure assessment (SOFA) score, and clinical pulmonary infection score (CPIS) were evaluated within 24 hours. The definition of chronic infection was considered to be a positive sputum culture for this isolate on at least three occasions over a six-month period, as previously suggested [12].

Microorganism identification and antimicrobial susceptibility testing

All strains were isolated from sputum or tracheal aspirate. All strains were identified using the API 20 NE system (bioMerieux Vitek, Marcy l'Etoile, France) and the VITEK II system(bioMerieux Inc., Hazelwood, USA) in accordance with reported techniques. In the clinical laboratory, a bacterial sensitivity test was performed using either the VITEK or micro-broth dilution method as described previously [13]. The results were interpreted using the Clinical and Laboratory Standards Institute (CLSI) guidelines [14].

Case-control study design

Based on the antimicrobial susceptibility testing, all patients were divided at a 1:1 ratio into two groups: imipenem resistant and imipenem nonresistant. Clinical information including basic demographics, underlying diseases, intubation, antimicrobial use within 14 days,

Table 1. Clinical features of the patients with*Achromobacter xylosoxidans* infection.

Clinical features	Total number	Number of positive cases	Positive rate (%)
Gender, male	41	38	92.7
Age, years, average ± SD (range)		87.3 ± 5.6 (74–99)	
Clinical manifestations			
Fever	41	26	63.4
Chill	41	6	14.6
Purulent sputum	41	39	95.1
Rale	41	32	78.0
WBC count > 10×10^9/L	41	20	48.8
Neutrophils > 70%	41	34	82.9
Platelets < 100×10^9/L	41	15	36.6
Anemia	41	37	90.2
Elevated CRP	40	39	95.1
Serum albumin	41	31	75.6
Chest imaging			
Unilateral exudation	41	24	58.5
Bilateral exudation	41	17	41.5
Unilateral pleural effusion	41	14	34.1
Bilateral pleural effusion	41	3	7.3
Consolidation	41	2	4.9
APACHE II (mean ± SD)			23.66 ± 7.71
CPIS (mean ± SD)			7.66 ± 1.57
SOFA (mean ± SD)			6.93 ± 2.47
Mortality	41	9	22.0

WBC: white blood cells; CRP: C-reactive protein; APACHE II: acute physiology and chronic health evaluation II; CPIS: clinical pulmonary infection score; SOFA: sequential organ failure assessment

previous use of immunosuppressants, chemotherapy, antacid use, clinical score, and mortality rate were compared and analyzed.

Statistical analysis

To examine the characteristics of all patients, measurement data were assessed as mean ± standard deviation (SD), and count data were analyzed as percentages.

To determine risk factors for imipenem-resistant *A. xylosoxidans*, univariate logistic regression analyses were performed. To determine independent risk factors, a multivariate logistic regression analysis was performed ($p < 0.05$). All risk factors with p values < 0.05 in the univariate model were included in the multivariate model. All tests were two tailed [15]. $P < 0.05$ was considered significant. SPSS, version 19.0 (IBM, Armonk, USA) was used for the analysis.

Table 2. Underlying diseases and state of the hospital-acquired pneumonia patients with *Achromobacter xylosoxidans* infection.

Underlying diseases and state	Total number	Number of positive cases	Positive rate (%)
Underlying diseases			
Chronic heart diseases			
Coronary heart diseases	41	26	63.4
Hypertension	41	33	80.5
Arrhythmia	41	13	31.7
Chronic lung diseases			
COPD	41	13	31.7
Interstitial lung diseases	41	15	36.6
Tuberculosis	41	4	9.8
Cancers	41	8	19.5
Hematologic malignancies	41	1	2.4
Solid tumors	41	7	17.1
Cerebrovascular diseases	41	30	73.2
Chronic renal failure	41	6	14.6
Diabetes	41	21	51.2
Peptic ulcer	41	3	7.3
Antibiotics used in 14 days			
Cephalosporins	36	21	58.3
Carbapenem	36	13	36.1
Quinolones	36	12	33.3
Broad-spectrum penicillins	36	9	25.0
Aminoglycosides	36	4	11.1
Linezolid	36	2	5.6
Antifugal drugs	36	11	30.6
Nitroimidazole	36	9	25.0
Tetracycline	36	5	13.9
Trimethoprim-sulfamethoxazole	36	2	5.6
Catheterization			
Central venous catheterization	41	31	75.6
Nasotracheal intubation	41	7	17.1
Tracheostomy cannula	41	22	53.7
Ureter	41	21	51.2
Stomach tube	41	38	92.7
Drugs			
Proton-pump inhibitor	41	31	75.6
Corticosteroids	41	5	12.2
Chemotherapy	41	3	7.3
Immunosuppressor	41	2	4.9
Antacids	41	1	2.4
Operation			
Abdominal operation	41	2	4.9
Chest surgery	41	1	2.4

COPD: chronic obstructive pulmonary disease.

Results

Clinical features of all patients with A. xylosoxidans infection

The clinical features of the patients are summarized in Tables 1 and 2. The patients had a mean age of 87.3 ± 5.6 years, and 92.3% (38/41) were males. The most frequent underlying disease was hypertension, which was present in 33 (80.5%) patients. Thirty patients (73.2%) had cerebrovascular disease, 26 patients (63.4%) had coronary heart disease, and 21 patients (51.2%) had diabetes mellitus. Other underlying diseases were interstitial lung disease (15 patients, 36.6%), chronic obstructive pulmonary disease (COPD) (13 patients, 31.7%), arrhythmia (13 patients), malignancy (8 patients, 19.5%), chronic renal failure (6 patients), old pulmonary tuberculosis (4 patients), and peptic ulcer (3 patients). Thirty-one (75.6%) patients were being treated with a proton-pump inhibitor (PPI), and 5 (12.2%) patients were receiving corticosteroids. Three patients were undergoing chemotherapy, and two patients were receiving immunosuppressants. Moreover, almost all patients had undergone intubation. A stomach tube and central venous tube had been used in 92.7% (38/41) and 75.6% (31/41) of the patients, respectively. Other tubes that had been used were a nasotracheal tube (7 cases, 17.1%), tracheostomy cannula (22 cases, 53.7%), and urinary catheter (21 cases, 51.2%).

Thirty-six patients were treated with a variety of definitive antimicrobial therapies within 14 days: 58.3% (21/36) of the patients were prescribed cephalosporins, 36.1% (13/36) carbapenem, 33.3% (12/36) quinolones, and 30.6% (11/36) an antifungal drug. Other antibiotics included nitroimidazole (9 cases), broad-spectrum penicillin (9 cases), tetracycline (5 cases), aminoglycosides (4 cases), linezolid (2 cases), and trimethoprim-sulfamethoxazole (2 cases). The time at which a positive culture of the organism was obtained ranged from two weeks to three years after admission to the inpatient department.

Chest imaging of all patients revealed patchy exudation. Pleural effusion was found in 41.5% (17/41) of the patients, and 2 patients showed consolidation. The most notable finding was a lower rate of fever and an increase in white blood cell counts in fewer than half of the patients. However, nearly 90% of the patients presented increased numbers of neutrophils and elevated levels of C-reactive protein (CRP). In addition, in terms of biochemical markers, 37 patients (90.2%) had anemia (hemoglobin < 120 g/L), and 31 cases (75.6%) had decreased serum albumin levels (< 35 g/L) at onset.

Six patients had chronic infections that lasted more than one year. Among those patients with infection, 32 were alive and 9 (22.0%) had died 30 days after infection.

Antimicrobial susceptibility

The antimicrobial susceptibility is shown in Table3. All strains were resistant to nitrofurazone and almost all strains were resistant to gentamicin and amikacin. The resistance rate of aztreonam approached 90%.

Table 3. Antimicrobial susceptibility patterns of the *Achromobacter xylosoxidans* isolated in a tertiary hospital.

Drug	Resistance N (%)	Intermediate N (%)	Sensitive N (%)
Amikacin	40 (97.6%)	0 (0.0%)	1 (2.4%)
Gentamicin	40 (97.6%)	0 (0.0%)	1 (2.4%)
Aztreonam	37 (90.2%)	4 (9.8%)	0 (0.0%)
Cefoperazone	21 (51.2%)	9 (22.0%)	11 (26.8%)
Cefepime	25 (61.0%)	5 (12.2%)	11 (26.8%)
Ceftazidime	7 (17.1%)	5 (12.2%)	29 (70.7%)
Levofloxacin	9 (22.0%)	10 (24.4%)	22 (53.7%)
Ciprofloxacin	18 (43.9%)	9 (22.0%)	14 (34.1%)
Minocycline	3 (7.3%)	12 (29.3%)	26 (63.4%)
Imipenem	20 (48.8%)	3 (7.3%)	18 (43.9%)
Meropenem	15 (36.6%)	3 (7.3%)	23 (56.1%)
Cefoperazone/sulbactam	3 (7.3%)	5 (12.2%)	33 (80.5%)
Piperacillin	7 (17.1%)	2 (4.9%)	32 (78.0%)
Piperacillin-tazobactam	3 (7.3%)	1 (2.4%)	37 (90.2%)
Trimethoprim-sulfamethoxazole	6 (14.6%)	0 (0.0%)	35 (85.4%)
Polymyxin B	17 (41.5%)	1 (2.4%)	23 (56.1%)
Nitrofurantoin	41 (100.0%)	0 (0.0%)	0 (0.0%)

Table 4. Clinical features of the patients infected by imipenem-resistant *Achromobacter xylosoxidans*.

No.	Sex/age	Comorbidities	Cannula	Predisposing factor	Antibiotics used in 14 days	Clinical presentations	Chest imaging	Empiric therapy	Switched therapy	Mechanical ventilation	APACHE II	CPIS	SOFA	Complications	Outcome at 30 days
4	M/94	CHD; ILD; CRF; hypertension; cerebrovascular disease; malignancy	CVC; ureter; stomach tube; nasotracheal intubation	–	TZP; caspofungin	Fever (Tmax 39); chills; purulent sputum	Bilateral exudation; pleural effusion (R)	CIP	SCF	Non-invasive	31	10	10	Sepsis	Died
6	F/75	Hypertension; arrhythmia; diabetes; cerebrovascular disease; postoperative	CVC; ureter; stomach tube; tracheostomy cannula	PPI	–	Fever (Tmax 37.5); purulent sputum	Bilateral exudation; pleural effusion (R)	FEP	TZP	Invasive	23	6	8	RF	Survived
8	M/95	ILD; CHD; hypertension; arrhythmia; diabetes; cerebrovascular disease	CVC; stomach tube	PPI	–	Dyspnea; cyanosis; cough; purulent sputum	Bilateral exudation	Flomoxef	MXF	–	13	6	9	RF	Survived
16	M/85	Cerebrovascular disease; malignancy; hypertension; arrhythmia; CHD; COPD	Stomach tube; tracheostomy cannula	PPI	CIP; MEM	Fever (Tmax 38.7); chills; purulent sputum	Exudation (R)	SCF	SCF	–	32	7	7	–	Survived
17	M/82	CHD; diabetes; hypertension; cerebrovascular disease	CVC; stomach tube; tracheostomy cannula	PPI	TZP; SXT; MXF; linezolid; voriconazole	Fever (Tmax 38.7); chills; cough; purulent sputum	Exudation (R); pleural effusion (L)	SCF	TZP+MIN	Non-invasive	31	8	8	RF	Survived
18	M/90	COPD; CHD; CRF; diabetes; hypertension; arrhythmia; cerebrovascular disease	CVC; ureter; stomach tube; tracheostomy cannula	PPI; corticosteroids	MXF; linezolid; voriconazole	Purulent sputum	Bilateral exudation	IPM	TZP	Non-invasive	28	8	7	RF	Survived
21	M/92	CHD; CRF; diabetes; hypertension; arrhythmia	CVC; ureter; stomach tube; nasotracheal intubation	PPI	MEM; MXF; omidazole	Purulent sputum	Bilateral exudation; Pleural effusion (L)	SCF		Non-invasive	31	8	11	RF	Survived
22	M/91	COPD; CHD; hypertension; arrhythmia; malignancy	CVC; ureter; stomach tube; tracheostomy cannula	PPI	MEM; FEP	Fever (Tmax 37.5); purulent sputum	Exudation (R); pleural effusion (R)	CAZ	LEV+MEM	Non-invasive switched to invasive	32	8	6	RF	Survived
23	M/93	COPD; CHD; CRF; diabetes; hypertension; cerebrovascular disease	CVC; ureter; stomach tube; tracheostomy cannula	PPI	MXF; linezolid; voriconazole	Fever (Tmax 38.5); chills; purulent sputum	Bilateral exudation	IPM	LEV+TZP	Invasive	35	8	12	Sepsis	Died
24	M/88	COPD; ILD; CHD; diabetes; hypertension; cerebrovascular disease	CVC; ureter; stomach tube; tracheostomy cannula	PPI	MEM; penicillin	Purulent sputum	Exudation	IPM	LEV+SCF	Non-invasive switched to invasive	20	8	6	RF	Survived

Table 4*(continued)*. Clinical features of the patients infected by imipenem-resistant *Achromobacter xylosoxidans*.

No.	Sex/age	Comorbidities	Cannula	Predisposing factor	Antibiotics used in 14 days	Clinical presentations	Chest imaging	Empiric therapy	Switched therapy	Mechanical ventilation	APACHE II	CPIS	SOFA	Complications	Outcome at 30 days
26	M/87	COPD; ILD; hypertension; CHD; cerebrovascular disease	CVC; ureter; stomach tube; tracheostomy cannula	PPI	SCF; IPM; linezolid	Purulent sputum	Exudation (R)	MEM	CIP+TZP	–	18	8	6	–	Survived
27	M/91	COPD; CHD; hypertension; diabetes	CVC; ureter; stomach tube; tracheostomy cannula	PPI	FEP; TZP	Cough; purulent sputum	Exudation (R)	MEM	CAZ+MIN	–	18	7	7	–	Survived
31	M/87	CHD; hypertension; cerebrovascular disease	CVC; ureter; stomach tube; tracheostomy cannula	PPI	CSF; etimicin; flomoxef	Fever (Tmax 37.9); purulent sputum	Exudation (L)	MEM	TZP+CAZ	Invasive	33	6	10	Sepsis	Died
33	M/79	COPD; ILD; CHD; diabetes; hypertension; cerebrovascular disease	Stomach tube; nasotracheal intubation	PPI; corticosteroids	IPM; MIN; TZP	Purulent sputum	Exudation (L)	MXF	SCF	–	18	7	5	–	Survived
34	M/83	COPD; ILD; CHD; hypertension; arrhythmia; cerebrovascular disease	CVC; stomach tube; tracheostomy cannula	PPI	TZP; SXT; voriconazole	Fever (Tmax 38.5); purulent sputum	Exudation (L); pleural effusion (R)	CAZ+CIP	SCF	Non-invasive switched to invasive	33	11	8	Septic shock	Died
35	M/88	ILD; OPT; HD; diabetes; cerebrovascular disease	–	–	–	Cough; purulent sputum	Exudation (R)	MXF		–	16	8	6	RF	Survived
36	M/99	COPD; diabetes; cerebrovascular disease	CVC; ureter; Stomach tube; tracheostomy cannula	PPI	SCF; MEM	Purulent sputum	Exudation (R)	IPM	MIN+TZP	Non-invasive switched to invasive	21	7	7	RF	Survived
38	M/88	CRF; hypertension; peptic ulcer; cerebrovascular disease; malignancy	CVC; ureter; stomach tube; tracheostomy cannula	PPI; H2 receptor blockers	CAZ; MEM; caspofungin; MNZ	Fever (Tmax 38.0); cough; chills; purulent sputum	Bilateral exudation	LEV	TZP	–	32	10	7	Sepsis	Died
39	F/82	Diabetes; cerebrovascular disease; hypertension	CVC; ureter; stomach tube; nasotracheal intubation	PPI; corticosteroids	MEM; FEP; caspofungin	Fever (Tmax 37.4); purulent sputum	Exudation (R); pleural effusion (L)	MXF	CSF+CAZ	Non-invasive switched to invasive	30	10	8	Sepsis	Died
41	M/93	CHD; arrhythmia; hypertension	CVC; ureter; stomach tube; tracheostomy cannula	PPI; corticosteroids	MIN; IPM; CSF; MNZ	Fever (Tmax 37.6); purulent sputum	Bilateral exudation; pleural effusion (L)	MEM	CIP+TZP	Invasive	27	6	6	RF	Survived

CHD: coronary heart disease; COPD: chronic obstructive pulmonary disease; ILD: interstitial lung disease; CRF: chronic renal failure; OPT: obsolete pulmonary tuberculosis; RF: respiratory failure; CVC: central venous catheterization; PPI: proton-pump inhibitor; TZP: piperacillin-tazobactam; SCF: cefperazone-sulbactam; SXT: trimethoprim-sulfamethoxazole; IPM: imipenem; MEM: meropenem; FEP: cefepime; MIN: minocycline; MNZ: metronidazole; CAZ: ceftazidime; MXT: moxifloxacin; CIP: ciprofloxacin; LEV: levofloxacin; APACHE II: acute physiology and chronic health evaluation II; CPIS: clinical pulmonary infection score; SOFA: sequential organ failure assessment.

Approximately half of the isolates were resistant to carbapenems, polymyxin B, quinolone, and third- and fourth-generation cephalosporins (excluding ceftazidime). However, significant sensitivity to minocycline, piperacillin-tazobactam, and cefoperazone-sulbactam was observed.

Clinical features and risk factors of patients with imipenem-resistant A. xylosoxidans infection

The detailed clinical and microbiological data for the 20 cases of imipenem-resistant infection are described in Table 4. Compared with patients with imipenem-nonresistant *A. xylosoxidans* (Table 5), more patients with imipenem-resistant *A. xylosoxidans* had received long-term catheterization (tracheostomy cannula), a PPI, or had COPD or CHD. Among the four risk factors, both COPD and CHD persisted as independent risk factors in the multivariate analysis. Of 21 cases with imipenem-resistant infection, 3 had chronic infections that lasted for more than 1 year, and 6 had died 30 days after infection.

Discussion

This is the first report of HAP due to *A. xylosoxidans* in elderly patients in China. Most of the patients had three or more underlying diseases and had undergone two or three catheterizations. Invasive manipulation may increase the risk for infection since the airway epithelial cells may be damaged, which could greatly reduce the defensive capabilities of the patient. Old age and high rates of cerebrovascular disease may have greatly increased the risk of aspiration due to reduced sensitivity of pharyngeal reflex [15].

In our study, 92.7% (38/41) of the patients received nourishment via a stomach tube. In addition, 75.6% (31/41) patients had decreased albumin, which may be one explanation for the poor immune response. Moreover, 51.2% (21/41) patients had diabetes, which is a known risk factor for infection [16]. In addition, the patients with CHD were classified as New York Heart Association (NYHA) functional class (FC) IV, which is one explanation for the long-term bed-ridden status. In summary, the influence of these comorbidities on one another may have contributed to the development of infection.

In the present study, it was notable that the rate of chemotherapy, use of glucocorticoids, and use of other immunosuppressants was reduced, but the rate of PPI use was nearly 80%. Almost all the elderly patients had a stomach tube to obtain nutrition, and antiplatelet drugs were frequently used to treat cardiovascular and cerebrovascular diseases. Therefore, PPI was used to prevent gastrorrhagia and peptic ulcer. Many studies have shown that PPI use may greatly increase the risk of infection due to the low pH of the stomach mucous [17]. Furthermore, PPI can reduce the minimum inhibitory concentration (MIC) of some antibiotics [18].

Most of the patients had anemia and decreased albumin levels due to undernutrition, which may lead to a reduced rate of fever and increased white blood cell (WBC) numbers. Interestingly, N% (neutrophil percent) and CRP show higher sensitivity in elderly patients, which is largely consistent with previous findings [19] and thus may be characteristic of the elderly.

Compared with a previous study, the APACHE II score (23.66 ± 7.71) was higher in the present analysis, which was mainly a result of old age [20]. Mortality was related to *A. xylosoxidans* infection in nine (22%) patients, which is similar to previous findings [20,21]. Aisenberg *et al*. collaborators [20] revealed that sepsis syndrome and high APACHE II scores are predictors of an increase in 30-day mortality. Although the APACHE II score in the imipenem-resistant group (26.95 ± 8.02) was higher than that in the imipenem-nonresistant group (20.52 ± 6.06) ($p < 0.05$), there were no obvious differences in mortality (6 cases versus 3 cases). This finding may be due to the small sample size.

Other epidemiological studies have demonstrated that outbreaks due to this organism can be associated with intravascular pressure [22] transducers and chlorhexidine [23]. However, due to the limitations of this retrospective study, this isolate was not identified in routine detection of the doctor's hands and medical instruments in the infectious diseases department.

A previous study has shown that most of the isolates are susceptible to trimethoprim-sulfamethoxazole, piperacillin-tazobactam, and cefoperazone-sulbactam, and are resistant to second- and third-generation cephalosporins, aminoglycosides, and ciprofloxacin. However, the strains in the present study showed increased sensitivity to minocycline, and approximately half of the isolates were resistant to imipenem. Moreover, 17 isolates (33.3%) were resistant to polymyxin B. In addition, all patients were highly resistant to nitrofurantoin, which is used to treat urinary tract infections. Thus, if this organism is detected in urine cultures, doctors should be alerted to avoid the spread of infection. The increasing numbers of antibiotic-resistant organisms was more frequently detected, and the repeated administration of antibiotics to treat infections due to common pathogens, especially

P. aeruginosa and *A. baumannii*, might underlie the selection for resistant *A. xylosoxidans* [24].

As a result of this, synergistic antimicrobial combinations have been evaluated. Previous studies have shown that piperacillin plus gentamicin [25], azithromycin plus doxycycline, and azithromycin plus trimethoprim-sulfamethoxazole may provide treatment alternatives for infections caused by multidrug-resistant *A. xylosoxidans* [26].

Carbapenems are active against many clinically widespread pathogens and are stable in the presence of various β-lactamases, especially for the treatment of a wide variety of multidrug-resistant pathogens. To date, many reports have shown a widespread epidemic of carbapenem-resistant isolates. Moreover, various metallo-b-lactamase (MBL) were detected, suggesting that *Achromobacter* spp. became a reservoir of various resistance genes of storage and exchange. [10,27,28,29].

In the imipenem-resistant group, COPD and CHD were independent risk factors. CHD, especially NYHA FCIV, could result in elderly patients becoming bedridden, which could increase the rate of hypostatic pneumonia and, consequently, exposure to various antibiotics for persistent and recurrent infection. Respiratory infection is a common reason for acute exacerbation of COPD (AECOPD). The repeated useof antibiotics to treat underlying diseases may contribute to imipenem resistance. Thus, the rational use of antibiotics and prevention of infection for elderly patients who had various underlying diseases is of principal importance. Treatment is also a challenge because of the high rate of antibiotic resistance among the elderly. Some researchers recommend trimethoprim-sulfamethoxazole, carbapenems, and antipseudomonal penicillins (with or without an aminoglycoside) for the treatment of systemic infections[20]. However, half of our patients were resistant to carbapenems. Considering the renal toxicity of trimethoprim-sulfamethoxazole, it is suggested that minocycline, piperacillin-tazobactam, and cefoperazone-sulbactam may be the best choice for the treatment of elderly patients. However, one report has indicated that early treatment with inhaled antibiotics may prevent or postpone chronic infection due to *Achromobacter* in patients with CF [30]. Thus, this therapy may provide an alternative choice.

There are some limitations in our study. First, it consisted of a small sample, and our findings may not be exactly reflected for other populations. Second, it was a retrospective study, so molecular testing for isolates was not carried out, and we were unable to explain epidemiological issues.

Conclusions

Due to the lack of recognition of *A. xylosoxidans*, some cases have been considered to be contamination. If this isolate is detected in patients with CHD, COPD, or with indwelling catheters, great attention should be focused on hygiene during the handling of medical instruments, and the specimen should be cultured several times. When the strain causing infection in elderly patients has been identified, optimal antibiotic treatments and mechanical ventilation should be adopted in time.

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