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 cerebrospinal fluid [6-9], this organism has been gradually accepted as an opportunistic and emerging pathogen that 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*<sub>IMP</sub> 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, 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].

### 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 × 10⁹/L             | 41           | 20                       | 48.8              |
| Neutrophils > 70%                  | 41           | 34                       | 82.9              |
| Platelets < 100 × 10⁹/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               |
| Antifungal 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 Table 3. All strains were resistant to nitrofurazone and almost all strains were resistant to gentamicin and amikacin. The resistance rate of aztreonam approached 90%.

| 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 | Mechanica l ventilation | APACH E II | CPI | SOF | Complication(s) | Outcome at 30 days |
|-----|---------|---------------|---------|--------------------|-----------------------------|------------------------|---------------|----------------|----------------|----------------------|-----------|-----|-----|-----------------|-----------------|
| 4   | M/94    | CHD; ILD; hypertension; cerebrovascular disease; malignancy | CV/C; 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; diabetes; cerebrovascular disease; postoperative ILD; CHD; hypertension; arrhythmia; diabetes; cerebrovascular disease | CV/C; 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    | Hypertension; diabetes; cerebrovascular disease | CV/C; stomach tube | PPI | – | Dyspnea; cyanosis; cough; purulent sputum | Bilateral exudation | Flomoxef | MXF | – | 13 | 6 | 9 | RF | Survived |
| 16  | M/85    | 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    | Hypertension; cerebrovascular disease | CV/C; 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    | Hypertension; arrhythmia; cerebrovascular disease | CV/C; 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    | Hypertension; arrhythmia | CV/C; ureter; stomach tube; nasotracheal intubation | PPI | MEM; MXF; omizidazole | Purulent sputum | Bilateral exudation; Pleural effusion (L) | SCF | – | Non-invasive | 31 | 8 | 11 | RF | Survived |
| 22  | M/91    | Hypertension; arrhythmia; malignancy | CV/C; ureter; stomach tube; tracheostomy cannula | PPI | MEM; FEP | Fever (Tmax 37.5); purulent sputum | Exudation (R); pleural effusion (R) | CAZ | LEV+ME M | Non-invasive switched to invasive | 32 | 8 | 6 | RF | Survived |
| 23  | M/93    | Hypertension; cerebrovascular disease | CV/C; 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    | Hypertension; cerebrovascular disease | CV/C; 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; CHD; 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    | COPD; ILD; CHD; diabetes; cerebrovascular disease | Stomach tube; nasotracheal intubation | PPI; corticosteroids | IPM; MIN; TZP | Purulent sputum | Exudation (L) | MXF | SCF | – | 18 | 7 | 5 | – | Survived |
| 33  | M/79    | COPD; ILD; CHD; hypertension; 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    | COPD; ILD; CHD; hypertension; cerebrovascular disease | – | – | – | Cough; purulent sputum | Exudation (R) | MXF | – | – | 16 | 8 | 6 | RF | Survived |
| 36  | M/99    | COPD; 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    | COPD; 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 gastorrhhagia 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 use of 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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