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Full Length Research Paper

Clinical and epidemiological description of Imipenem-resistant *Acinetobacter baumannii* causing nosocomial infections in a regional teaching hospital in China

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To elucidate the clinical characteristics of imipenem-resistant *Acinetobacter baumannii* causing nosocomial infections in the First Affiliated Hospital of China Medical University, 34 isolates genotyped by pulsed-field gel electrophoresis (PFGE) were collected from January 2007 to December 2007. Isolates were most commonly found in the ICU and burn ward in this study, accounting for 47.06% (16 isolates) and 26.47% (9 isolates) of the total isolates, respectively. For the most patients infected by *A. baumannii*, three to seven risk factors generally existed. But some factors (including diabetes mellitus, chronic respiratory diseases and tumor) were mostly negative for those patients. The clinical data obtained suggested that the three clinical risk factors may take little action in the nosocomial infection caused by *A. baumannii*s in the hospital. As for the use of antimicrobial, different types were selected before the occurrence of the most infections. This may be an important factor leading to the multi-drug resistance.

Key words: Acinetobacter baumannii, clinical characteristics, epidemiological description, risk factors.

INTRODUCTION

Initial concerns about imipenem-resistant *Acinetobacter baumannii* (*A. baumannii*) arose when the first nosocomial outbreak occurred in the United States in 1991 (Go et al., 1994). Not unexpectedly, clinical outbreaks attributable to imipenem-resistance *A. baumannii* strains have been increasing in frequency (Héritier et al., 2005; Jeon et al., 2005; Vahaboglu et al., 2006). Previous studies have revealed the usefulness of molecular typing in defining the epidemiologic significance of clusters of *A. baumannii* isolates (Go et al., 1994; Kaul et al., 1996; Patterson et al., 1991; Villers et al., 1998). The typing systems include ribotyping, amplified fragment length polymorphism, pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST), randomly amplified polymorphic DNA (RAPD), and infrequent-restriction-site PCR. PFGE has been used with excellent results in epidemiologic studies of numerous *A. baumannii* outbreaks and is currently regarded as the gold standard for epidemiologic typing. In our prior research, we have identified the molecular epidemiological typing of all the 34 isolates by both PFGE and MLST methods (Zhang et al., 2010). And the present study was undertaken to further document the clinical characteristics of 34 imipenem-resistant *A. baumannii* in a university hospital based on the result of molecular epidemiological typing. We attempt to find a solution to control the transmission of *A. baumannii* in the First Affiliated Hospital of China Medical University.

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MATERIALS AND METHODS

Bacteria

Thirty-four *A. baumannii* isolates were collected in the First Affiliated Hospital of China Medical University during the period from January 2007 to December 2007. These isolates were recovered from sputum specimens (24 isolates), secretion specimens (5 isolates), urine specimens (3 isolates), drainage fluid specimens (1 isolates), and a blood specimen (1 isolate). All the 34 isolates were defined as pathogenic bacteria that were directly responsible for the nosocomial infection. Isolates were identified, and initial antimicrobial susceptibilities were determined by the Vitek system (bioMerieux Marcy l'Etoile, France). Susceptibility was interpreted according to Clinical and Laboratory Standards Institute guidelines (CLSI, 2006). For imipenem (purchased from Merck, Whitehouse Station, NY, USA), the resistance breakpoint was defined as a inimum inhibitory concentrations (MICs) of 16 µg/ml. *Escherichia coli* ATCC25922 and *Pseudomonas aeruginosa* ATCC27853 were used as control strains. Antibiotic susceptibility testing revealed that all the strains were resistant to imipenem. The MICs of the isolates to imipenem ranged between 16 and 128 µg/ml, with the most common MIC being 32 µg/ml.

In our prior study, all 34 imipenem-resistant isolates were genotyped by *Apa*I digestion-PFGE analysis and categorized into four types (A-D). The A- and B-type were further divided into three and two subtypes, respectively, accounting for 47.06 and 41.18% of the strains, respectively. Additionally, the MLST results demonstrated the existence of three allelic profiles: 1-3-3-2-2-7-3 (A-type), 1-3-3-2-2-11-3 (B- and D-type), and 1-3-3-2-2-14-3 (C-type). The MLST data for all isolates were in high concordance with the epidemiological typing results generated by PFGE.

Collection of clinical data

The clinical data were collected from the medical records recorded by the doctors, including the following variables: age, source of specimen, detection time of isolates, ward, and major risk factors (e.g., ICU ward transfer, underlying diseases, types and duration of exposure to antimicrobials, urinary catheter, venous catheter, mechanical ventilation, nasogastric tube, prior surgery).

Definition

Patients with respiratory isolates were considered infected if they had evidence of pneumonia defined as the presence of a chest radiograph infiltrate plus at least 2 of the following criteria: fever (38.3°C), white blood count WBC>11.0 /mm^3, or positive blood culture for *A. baumannii*.

Prior antimicrobial use was defined as the use of a systemic antimicrobial agent for at least 72 h within the 2 weeks preceding the date of the positive-culture for bacteremic patients, or the date of discharge from the intensive care unit (ICU) for non-bacteremic patients.

RESULTS

Clinical data

We retrospectively analyzed the cases to collect the clinical data and identify the spatial and temporal distribution of the isolates. Isolates were most commonly found in the ICU and burn ward in this study (Table 1), accounting for 47.06% (16 isolates) and 26.47% (9 isolates) of the total isolates, respectively. The remaining nine isolates were found in the wards of respiratory, neurology, infection, cardiovascular, urology surgery, cardiac surgery, oncology surgery, and general surgery (each 1 or 2 strains). For the most patients, three to seven risk factors generally existed, but three factors (including diabetes mellitus, chronic respiratory diseases and tumor) were mostly negative (Table 1). As for the use of antimicrobial, different types were selected before the occurrence of the most infections.

DISCUSSION

With the widespread use of antibiotics, the multidrug resistance of *A. baumannii* is increasing (Gould 2008), which has been named "methicillin-resistant *Staphylococcus aureus* (MRSA)" in Gram-negative bacteria. In the past few years, outbreaks in the ICU have led to high numbers of fatalities (Garcia-Garmendia et al., 2001; Poirel and Nordmann et al., 2006). It has been proved that patient transfer and hospital staff contact may enhance the spread of imipenem-resistant *A. baumannii* among different wards. In order to further understand the clinical characteristics of different genotypes, based on the results of molecular epidemiological typing, we retrospectively analyzed those infectious cases.

From the distribution of spatial and temporal of the isolates, the ICU and burn unit were the main distribution areas in our hospital. Because of the multiple underlying diseases and risk factors such as invasive procedures, patients in the ICU tended to be infected with multiple resistant isolates. So the detection rate of multidrug resistant *A. baumannii* are usually the most highest in ICU ward at various levels. Combined with the results of our prior study, three different types of clonal isolates were separated from the ICU, including 15 A-type clones, 5 B-type clones, and 1 C-type clone. The burn ward was the only department where B- and D-type were detected. A-type was the main cloning type in ICU, and this may be the probably reason that A-type clones accounted for a major position of in the first affiliated hospital of China Medical University' A. baumannii. At the same time, A-type clones were distributed in a number of other wards. This illustrated that A-type isolates had been transmitted between different wards in the hospital, indicating the possibility of cross-infection between different wards. This transmission of A-type clones may have contributed to the increasing prevalence of imipenem-resistant isolates in the hospital. Before September 17, 2007, no patient infected with A1-type isolates in other wards was transferred to the ICU. Combined with the detection time of A1-type isolates in the ICU, this suggested the possibility of interward transmission. The study also

Table 1. Clinical and epidemiological description of 34 *A. baumannii* isolates.

No.	source of specimen	Age (year)	ward	PFGE	Clinical risk factor								
					PS	MV	UC	DM	CRD	tumor	VC	NT	PS
36	Sputum	76	ICU	A1	Y	Y	Y	N	N	Y	Y	Y	Y
41	Sputum	79	ICU	A1	Y	Y	Y	Y	Y	N	Y	Y	N
44	Sputum	43	ICU	A1	Y	Y	Y	N	N	N	Y	Y	N
47	Sputum	67	ICU	A1	Y	Y	Y	N	N	Y	Y	Y	Y
51	Sputum	75	ICU	A1	Y	Y	Y	Y	N	N	Y	Y	N
33	Sputum	75	ICU	A1	Y	Y	Y	N	Y	Y	N	Y	Y
48	Sputum	77	ICU	A1	Y	Y	Y	N	Y	N	Y	Y	Y
30	Sputum	72	Neurology ward	A1	Y	N	Y	Y	N	N	Y	Y	N
54	Sputum	65	Oncology surgery	A1	Y	Y	Y	N	N	Y	Y	Y	Y
7	Sputum	39	cardiac surgery	A1	N	Y	Y	Y	N	N	Y	Y	Y
57	Sputum	79	ICU	A2	Y	Y	Y	Y	Y	N	Y	Y	N
40	Sputum	78	ICU	A2	Y	Y	Y	N	N	N	Y	Y	N
28	Sputum	71	ICU	A2	Y	Y	Y	N	Y	Y	Y	Y	Y
58	Sputum	74	ICU	A2	Y	Y	Y	N	N	Y	Y	Y	Y
59	Sputum	74	Respiratory ward	A2	Y	Y	Y	N	N	Y	Y	Y	Y
35	Sputum	82	ICU	A3	Y	Y	N	N	N	Y	N	Y	Y
2	Blood	49	Burn ward	B1	Y	Y	Y	N	N	N	Y	Y	Y
11	Secretion	36	Burn ward	B1	Y	Y	Y	N	N	N	Y	Y	Y
16	Secretion	36	Burn ward	B1	Y	Y	Y	N	N	N	Y	Y	Y
18	Sputum	83	Burn ward	B1	Y	Y	Y	N	N	N	N	Y	Y
45	Sputum	74	General surgery	B1	N	N	Y	N	N	N	Y	N	N
26	Sputum	53	Urology surgery	B1	N	Y	Y	N	N	N	Y	Y	Y
4	Sputum	50	ICU	B1	Y	Y	Y	N	N	N	Y	Y	Y
50	Urine	45	Burn ward	B2	Y	Y	Y	N	N	N	Y	Y	Y
52	Urine	45	Burn ward	B2	Y	Y	Y	N	N	N	Y	Y	Y
17	Secretion	36	Burn ward	B2	Y	Y	Y	N	N	N	Y	Y	Y
3	Secretion	53	Burn ward	B2	Y	Y	Y	N	N	N	Y	Y	Y
14	Sputum	72	Respiratory ward	B2	Y	Y	Y	Y	N	N	Y	Y	Y
8	Sputum	16	ICU	B2	Y	Y	Y	N	N	N	N	Y	Y
15	Drainage fluid	54	ICU	B2	Y	Y	Y	N	N	N	N	N	Y
56	Sputum	86	Infection department	C	N	N	N	N	Y	N	Y	Y	N
23	Secretion	55	ICU	C	N	N	N	N	N	N	N	N	Y
24	Urine	63	Burn ward	D	Y	Y	Y	Y	N	N	Y	Y	Y
22	Sputum	80	Cardiovascular ward	D	Y	Y	Y	N	N	N	N	N	Y

PIS, Prior ICU stay; MV, mechanical ventilation; UC, urinary catheter; DM, diabetes mellitus; CRD, chronic respiratory diseases; VC, venous catheter; NT, nasogastric tube; PS, prior surgery

found a new clone in the ICU (C-type), and its higher resistance illustrated the necessity of strengthening the disinfection and isolation measures under the special circumstances of the ICU.

Two types of clones (B-and D-type) were isolated from the burn ward, with the B-type being the most prevalent. Regarding the B-type clones, B1- and B2-type were initially detected in the ICU and respiratory ward, respectively. Because the two patients were not switched to the burn ward, this suggested the possibility of transmission within wards. However, the possibility of transmission through the hands of medical staff could not be completely disproven. Therefore, to control the local prevalence of nosocomial clones, in addition to strengthening the disinfection and isolation measures, the importance of hand hygiene should be stressed, along with strengthening the rational use of antimicrobial agents based on characteristics of resistant isolates to prevent the increasing drug resistance of isolates.

It has been proven that risk factors for colonization/

Table 2. The types and duration of exposure to antimicrobials

No. of the Isolates	Types	Total duration (days)
15	5	53
57	4	30
52	4	19
7,36	3	25
41	3	20
48	3	33
35	3	30
50	3	21
3,24	3	19
14	3	13
22	3	16
2	2	24
17	2	12
8	2	21
44,54	1	3
47,51	1	4
30	1	8
58	1	13
16,18	1	7
56	1	6
4,11,23,26,28,33,40,45,59	0	0

infection with multidrug-resistant *A. baumannii* include prolonged length of hospital stay, exposure to an ICU, mechanical ventilation, colonization pressure, exposure to antimicrobial agents, recent surgery, invasive procedures, and underlying illness (Fournier and Richet, 2006; Playford et al., 2007). In this study, such risk factors were collected. In contrast to the other risk factors, underlying illness (including diabetes mellitus, chronic respiratory diseases, and tumor) only existed in a few patients (Table 1). For most patients, three to seven risk factors generally existed. As for the use of antimicrobial, most of the patients were identified the use of antimicrobial before the occurrence of infection (Table 2). This may be an important factor leading to the multi-drug resistance. At present, therapeutic options are limited for imipenem-resistant isolates. Therefore, once high-resistance bacterial isolates are detected, clinicians and administrative staff should work closely together. Effective preventive measures should be implemented promptly to prevent the nosocomial spread of epidemic resistant isolates.

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