Original Article

Distribution and drug resistance of pathogenic bacteria isolated from cancer hospital in 2013

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Objective: To understand distribution and drug resistance of pathogenic bacteria from a specialized cancer hospital in 2013 in order to provide a basis for rational clinical antimicrobial agents.

Methods: Pathogenic bacteria identification and drug sensitivity tests were performed with a VITEK 2 compact automatic identification system and data were analyzed using WHONET5.6 software.

Results: Of the 1,378 strains tested, 980 were Gram-negative bacilli, accounting for 71.1%, in which *Klebsiella pneumonia*, *Escherichia coli* and *Pseudomonas aeruginosa* were the dominant strains. We found 328 Gram-positive coccus, accounting for 23.8%, in which the amount of *Staphylococcus aureus* was the highest. We identified 46 fungi, accounting for 4.1%. According to the departmental distribution within the hospital, the surgical departments isolated the major strains, accounting for 49.7%. According to disease types, lung cancer, intestinal cancer and esophagus cancer were the top three, accounting for 20.9%, 17.3% and 14.2%, respectively. No strains were resistant to imipenem, ertapenem or vancomycin.

Conclusions: Pathogenic bacteria isolated from the specialized cancer hospital have different resistance rates compared to commonly used antimicrobial agents; therefore antimicrobial agents to reduce the morbidity and mortality of infections should be used.

Keywords: Tumor; pathogenic bacteria; distribution; drug resistance rate

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Introduction

To understand the characteristics of the pathogenic bacteria's distribution and drug resistance, it was helpful to control and prevent the occurrence of drug-resistant bacteria. A lot of reports in general hospitals were searched with this drug resistance criterion. Lower immunity, longer admission time, and different cancers were characterized in addition to radiation, chemotherapy, and invasive diagnostic factors, such as operations for cancer patients which can lead to increased incidence of infections. In addition, to prevent infection, preventive and therapeutic using of high doses of antimicrobial agents easily lead to ecological imbalance endogenous flora, and multiple sites of infection in the tumor patients (1,2). According to the literature, mortality rate of tumor patients increased due to infectious diseases (3,4). Many data showed that the treatment efficiency significantly decrease in some tumor patients owing to infection (5). Therefore, it is very important to treat infection timely in tumor patients. So it was necessary to illustrate pathogenic bacteria distribution and drug resistance in order to provide the basis for antimicrobial agent therapy for tumor patients.

Materials and methods

Strains

A total of 1,378 strains of pathogenic bacteria were isolated from all types of specimens in all the departments of Peking

University Cancer Hospital in 2013 (excluding the same repetitive strains from the same patient parts). The types of specimen included sputum, tracheal fluid, urine, blood, secretions, puncture drainage, fester, and so on.

Table 1 Distribution of 1,378 pathogens

Pathogen	Strains	Constituent ratio (%)
Gram-negative bacterium	980	71.1
Klebsiella pneumonia	291	21.1
Escherichia coli	220	16.0
Pseudomonas aeruginosa	181	13.1
Acinetobacter baumanmii	91	6.6
Escherichia cloacae	75	5.4
Proteus mirabillis	33	2.4
Others	89	6.5
Gram-positive bacterium	328	23.8
Staphylococcus aureus	92	6.7
Enterococcaceae faecium	42	3.0
Staphylococcus epidermidis	40	2.9
Staphylococcus haemolyticcus	25	1.8
Enterococcaceae faecalis	23	1.7
Others	106	7.7
Fungi	56	4.1
Candida albicans	38	2.8
Candida tropicalis	7	0.5
Others	11	0.8
Anaerobe	14	1.0

Instruments and reagents

Pathogenic bacteria identification and drug susceptibility tests were performed with a VITEK 2 compact automatic identification system (bioMérieux Inc., Marcy I'Etoile, France). Fungal susceptibility was determined by ATB FUNGUS3 (bioMérieux Inc., Marcy I'Etoile, France). Drug susceptibility results refer to the standards (M100-S24) of Clinical and Laboratory Standards Institute (CLSI) in 2014.

Quality control strains

Staphylococcus aureus (ATCC 29213), *Streptococcus pneumoniae* (ATCC 49619), *Escherichia coli* (ATCC 25922), *Enterobacter cloacae* (ATCC 70032), and *Candida albicans* (ATCC 90028) were purchased from the quality control center of the ministry of health of China.

Statistical analysis

Data were analyzed using WHONET 5.6 software (World Health Organization Collaborating Centre for Surveillance of Antimicrobial Resistance).

Results

Pathogenic bacteria specimen distribution ratios in tumor patients

A total of 1,378 strains were detected from 4,530 specimens; among which 787 strains were isolated from the respiratory tract, accounting for 57.1%; 160 strains from blood, accounting for 11.6%; 89 strains from secretion, accounting for 6.5%; 71 strains from urine, accounting for 5.2%; 33 strains from puncture fluid, accounting for 2.4%; 32 strains from catheter, accounting for 2.3%; and 31 strains from fester, accounting for 2.2%.

Tumor pathogenic bacteria distribution

Of the 1,378 strains, 980 Gram-negative bacilli were detected, accounting for 71.1%, in which *Klebsiella pneumonia*, *Escherichia coli* and *Pseudomonas aeruginosa* were dominant. We found 328 Gram-positive coccus, accounting for 23.8%, in which the amount of *Staphylococcus aureus* was the highest. We identified 46 fungi, accounting for 4.1%, and 14 strains were anaerobic bacteria, accounting for 1.0% (*Table 1*).

Department distribution

Of the 1,378 strains, the surgical departments detected 685 strains, accounting for 49.7%; the internal medicine departments detected 336 strains, accounting for 24.4%; the intensive care unit (ICU) detected 110 strains, accounting for 8.0%; the radiation department detected 95 strains, accounting for 6.9%; the interventional department detected 42 strains, accounting for 3.0%; and the Outpatient Service detected 110 strains, accounting for 8.0% (*Table 2*).

Cancer type distribution

Of the 1,378 strains, there were 288 cases of lung cancer,

Table 2 Distribution of 1,378 pathogens according to departments

Department	Strains	Constituent ratio (%)
Surgical departments	685	49.7
Department of Thoracic Surgery	283	20.5
Department of Hepato-pancreatic Biliary Surgery	158	11.5
Department of Gastrointestinal Surgery	131	9.5
Department of Orthopedic Oncology	88	6.4
Breast Cancer Center	25	1.8
Internal medicine departments	336	24.4
Department of Thoracic Medical Oncology	78	5.7
Department of Lymphoma	55	4.0
Department of Integration of Chinese and Western Medicine	45	3.3
Department of Breast Cancer	39	2.8
Department of Renal Cancer and Melanoma	36	2.6
Department of Transplant	30	2.2
Department of Gastrointestinal Oncology	27	2.0
Department of Gynecology	26	1.9
ICU	110	8.0
Department of Radiation Oncology	95	6.9
Department of Interventional Therapy	42	3.0
Outpatient	110	8.0

ICU, intensive care unit.

Table 3 Distribution of 1,378 pathogens according to tumor types

Type of tumor	Strains	Constituent ratio (%)
Lung cancer	288	20.9
Intestinal tumor	238	17.3
Esophageal cancer	195	14.2
Gastric cancer	157	11.4
Lymphadenoma	96	7.0
Breast cancer	54	3.9
Pancreatic cancer	49	3.6
Liver cancer	45	3.3
Malignant melanoma	36	2.6
Cholangiocarcinoma	24	1.7
Cervical cancer	23	1.7
Others*	173	12.6

*, others include kidney cancer, nasopharyngeal carcinoma, osteosarcoma, bladder cancer, ovarian cancer, etc., and all less than ten cases.

accounting for 20.9%; 238 cases of intestinal tumor, accounting for 17.3%; 195 cases of esophageal cancer, accounting for 14.2%; 157 cases of gastric cancer, accounting for 11.4%; 96 cases of lymphoma, accounting for 7.0%; and 54 cases of breast cancer, accounting for 3.9%, as shown in the *Table 3*.

Drug resistance results

Common Gram-negative bacteria resistance rates

Forty-one of *Klebsiella pneumoniae* produced extend spectrum beta lactamase (ESBLs), accounting for 14.1%; and 150 of *Escherichia coli* produced ESBLs, accounting for 68.2%. *Klebsiella pneumoniae* and *Escherichia coli* were not resistant to imipenem and ertapenem. The resistance rates to imipenem in *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were 14.9% and 13.2%, respectively (*Table 4*).

Table 4 Drug resistance of the main Gram-negative bacteria

Drug	*K. pneumonia* (n=291)				*E. coli* (n=220)				*P. aeruginosa* (n=181)		*A. baumanmii* (n=91)	
	ESBLs+ (n=41)		ESBLs− (n=250)		ESBLs+ (n=150)		ESBLs− (n=70)					
	Strain	DRR (%)	Strain	DRR (%)	Strain	DRR (%)	Strain	DRR (%)	Strain	DRR (%)	Strain	DRR (%)
Ampicillin	41	100	199	79.6	150	100	53	75.0	181	100	38	41.8
Cefazolin	36	87.8	11	4.4	150	100	15	20.8	181	100	91	100
Ceftriaxone	34	82.9	2	0.8	149	99.3	8	9.7	181	100	91	100
Ampicillin/ sulbactam	30	73.2	6	2.4	102	68.0	18	25.0	181	100	9	9.9
Trimethofrim/ sulfamethoxazole	28	68.3	12	4.8	109	72.7	4	4.7	175	96.7	7	7.7
Gentamicin	24	58.5	3	1.2	96	64.0	36	51.4	4	2.2	11	12.1
Aztreonam	22	53.7	3	1.2	92	61.3	8	11.1	–	–	91	100
Nitrofurantoin	18	43.9	35	14.0	5	3.3	1	1.4	179	98.9	91	100
Ceftazidime	12	29.3	2	0.8	62	41.3	8	11.1	7	3.9	9	9.9
Levofloxacin	11	26.8	3	1.2	96	64.0	33	47.2	12	6.6	9	9.9
Ciprofloxacin	11	26.8	2	0.8	104	69.3	51	51.4	9	5.0	9	9.9
Cefepime	7	17.1	1	0.4	34	22.7	6	8.3	3	1.7	10	11.0
Tobramycin	4	9.8	1	0.4	28	18.7	7	9.7	0	0.0	10	11.0
Piperacillin/ tazobacta	2	4.9	1	4.0	0	0	3	4.2	3	1.7	10	11.0
Amikacin	1	2.4	0	0	4	2.7	2	2.8	1	0.6	–	–
Ertapenem	0	0	0	0	0	0	0	0	–	–	–	–
Imipenem	0	0	0	0	0	0	0	0	27	14.9	12	13.2
Cefotetan	0	0	0	0	1	0.7	4	5.6	178	98.3	91	100
Meropenem	–	–	–	–	–	–	–	–	21	11.6	–	–

K. pneumonia, *klebsiella pneumonia*; *E. coli*, *escherichia coli*; *P. aeruginosa*, *pseudomonas aeruginosa*; *A. baumanmii*, *acinetobacter baumanmii*; DRR, drug resistance rate.

Common Gram-positive bacteria resistance rates

Staphylococcus aureus and *Enterococcus were* resistant to linezolid, but vancomycin resistance was not found (*Table 5*).

Fungal resistance rates

Itraconazol had the highest resistance percentage of 13.7% out of the 51 fungi (*Table 6*).

Discussion

Peking University Cancer Hospital is a specialized hospital. The patients admitted into this hospital have lower immune systems. High doses of multiple concurrent chemo-radiation can increase the chances of pathogenic bacteria invasion in most of the cancer patients hospitalized. As a result, nosocomial infections are sensitive to these types of patients. Moreover, radiation, chemotherapy, and long-term use of antibiotics lead to dysbacteriosis, which increases conditional pathogenic bacteria infections. Therefore, it is important to understand pathogenic bacteria and their drug resistance in patients with tumors for the initial clinical treatment experience and prognosis improvement.

Through the retrospective analysis of pathogenic bacteria performed in 2013, a total of 1,378 strains were detected. Respiratory specimens were the most prevalent (57.1%), followed by blood specimens (11.6%). Gram-negative bacteria and Gram-positive bacteria accounted for 71.1% and 23.8%, respectively, which was similar to the results of 2012 CHINET surveillance of bacterial resistance

Table 5 Drug resistance of the main Gram-positive cocci

Drug	*Staphylococcus aureus* (n=92)				*Enterococcus* (n=65)	
	MRSA (n=30)		MSSA (n=62)			
	Strain	DRR (%)	Strain	DRR (%)	Strain	DRR (%)
Penicillin G	30	100	51	82.3	22	33.8
Erythromycin	28	93.3	34	54.8	49	75.4
Clindamycin	28	93.3	33	53.2	59	90.8
Trimethofrim/sulfamethoxazole	7	23.3	21	33.9	–	–
Tetracycline	4	13.3	14	22.6	53	81.5
Gentamicin	5	16.7	13	21.0	–	–
Quinupristin/dalfopristin	1	3.3	9	14.5	38	58.5
Ciprofloxacin	23	76.7	2	3.2	27	41.5
Levofloxacin	24	80.0	2	3.2	26	40.0
Moxifloxacin	24	80.0	1	1.6	29	44.6
Teicoplanin	0	0	0	0	0	0
Rifampicin	2	6.7	0	0	–	–
Oxacillin	30	100	0	0	–	–
Tigecycline	0	0	0	0	0	0
Nitrofurantoin	0	0	0	0	8	12.3
Linezolid	0	0	0	0	0	0
Vancomycin	0	0	0	0	0	0
Gentamicin high level	–	–	–	–	0	0
Streptomycin high level	–	–	–	–	0	0
Ampicillin	–	–	–	–	19	29.2

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; DRR, drag resistance rate.

Table 6 Drug resistance rates of *Candida albicans* strain

Drugs	Strains	Drag resistance rate (%)
Itraconazole	7	13.7
Voriconazole	4	7.8
Fluconazole	3	5.9
Amphotericin	1	2.0
5-flucytosine	0	0

in China (6). The Gram-negative bacilli, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, were the top three bacteria detected, accounting for 21.1%, 16.0%, and 16.0%, respectively. The Gram-positive cocci, *Staphylococcus aureus* and *Enterococcus faecium*, were dominant, accounting for 6.7% and 3.0%, respectively. Li *et al.* reported that in Shandong Province Tumor Hospital, the top three detected gram-negative bacillus were *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *Escherichia coli*, and the top two Gram-positive bacteria were *Staphylococcus aureus* and *streptococcus pneumonia* (7). We proposed that the different pathogenic spectrum may be due to different cities, different hospitals, different geographical locations, and different operations and diseases. This research showed that fungi accounted for 4.1% of all pathogenic bacteria, which is slightly lower than the domestic reports (7). Fourteen strains of anaerobic bacteria accounted for 1.0%, among which *Bacteroides fragilis* was dominant.

In this study, the highest proportion of pathogens detected was in the surgical departments, due to more surgical inspection specimens and infection possibilities caused by operations, invasive diagnosis and treatments. Chest surgery had the highest detection because the patients with lung cancer were prone to lower respiratory tract infections and respiratory specimen collections. The internal medicine departments had a lower detection rate. Our study also found that the detection of pathogenic bacteria in lung cancer had the highest rate (20.9%), which was caused by impaired lung function in patients, especially in patients with advanced disease who stay in bed for a long time. In addition, chemotherapy and radiation decreased respiratory cilia functions, which decrease the function of clearing secretions and defense functions. Detection of pathogenic bacteria in intestinal tumors was secondary, accounting for 17.3%. It most likely caused intestinal infection or obstruction through surgery or tumor. Other tumors, such as breast cancer, liver cancer, pancreatic cancer and melanoma, had a lower detection rate of less than 4%.

According to the analysis of the drug resistance of pathogenic bacteria isolated from the hospital, *Klebsiella pneumoniae* and *Escherichia coli* were the top two detected, which produced ESBLs with a rate of 14.1% and 68.2%, respectively. The separation rate of ESBLs-positive *Klebsiella pneumoniae* was lower than the domestic reports, while the separation rate of ESBLs-positive *Escherichia coli* was higher than the domestic reports (6,8,9). Because of ESBLs encoding gene on a plasmid, its resistance can be through transformation, transduction, or translocation in different bacteria. Therefore, ESBLs-producing bacteria are often easy to carry on multiple drug resistance (10). Our data indicated that ESBLs-positive *Enterobacteriaceae* had a higher drug resistance rate than ESBLs-negative bacteria. The resistance rates to gentamicin, ampicillin/sulbactum, sulfanilamide, aztreonam and cephalosporin, except for cefepime and ceftazidime, were greater than 50.0% in ESBLs-positive *Klebsiella pneumonia*. The resistance rates to fluoroquinolone gentamicin, sulfanilamide, aztreonam and cephalosporin, except for cefepime and ceftazidime, were also more than 50%. Thus, caution should be taken to these drugs for treatment. Carbapenem had the highest sensitivity in *Enterobacteriaceae*. Our hospital did not demonstrate imipenem and ertapenem resistance in *Escherichia coli* and *Klebsiella pneumonia*. Piperacillin/sulbactum, amikacin, and cefotetan had higher sensitivity, so that they could be used for experience therapy.

Pseudomonas aeruginosa and *Acinetobacter baumannii* were the highest detected non-fermentative bacteria. *Pseudomonas aeruginosa* virulence was stronger and more prone to induced resistance; therefore, great attention should be paid. *Pseudomonas aeruginosa* had more than 90% sensitivity to piperacillin/sulbactum, amikacin, tobramycin, cefepime, cephalosporin, gentamicin, and fluoroquinolone, The resistance rates to imipenem and meropenem were 11.6% and 14.9%, respectively, which were lower than domestic reports (11). Pakyz *et al*. reported that *Pseudomonas aeruginosa* nosocomial isolation had a significant linear relationship with carbapenem usage. Restriction of carbapenem usage would reduce drug resistance occurrence (12). In addition, for *Pseudomonas aeruginosa* infection treatment, early effective antimicrobial therapy is crucial. Combination antimicrobial agents could play into the synergy of drugs and reduce the occurrence of drug resistance (13). Nosocomial infections with *Acinetobacter baumannii* and Methicillin-resistant *Staphylococcus aureus* (MRSA) were due to iatrogenic factors (medical personnel, medical apparatus and instruments, etc.) (14). In recent years, imipenem-resistant *Acinetobacter* has grown (15). *Acinetobacter baumannii* resistance rates to imipenem were 13.2% in our hospital. The resistance to cefepime, piperacillin/sulbactum, fluoroquinolone, gentamicin, cefazolin, tobramycin and sulfanilamide were less than 20.0%. Therefore, the treatment of non-fermentative bacteria should be performed according to the result of drug susceptibility and the abuse of antimicrobial agents should be avoided.

We did not find Gram-positive resistance to vancomycin, teicoplanin, or linezolid, which can be used as the drug of choice for serious *Staphylococcus* infections. *Staphylococcus* had more than a 50% resistance rate to the traditional antibacterial drugs such as penicillin, erythromycin, and clindamycin. Clinics should be careful to use these drugs. It should be pointed out that vancomycin and linezolid-resistant *Enterococcus faecalis* and *Enterococcus faecium* were not found.

Conclusions

Bacteria with antimicrobial resistance had strong regional differences; there are even differences between the hospitals. This study retrospectively analyzed all the whole 2013 bacteria resistance data to provide a scientific basis for choosing the right antibiotics in order to reduce the morbidity and mortality of infection.

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