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Original Article

Prognostic analysis of cancer patients with staphylococcus aureus infection: five-year experience at a comprehensive cancer center

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Abstract: Staphylococcus aureus (S. aureus) is one of the major pathogens in community and hospital-acquired bloodstream infections. However, few studies have focused on prognostic factors of cancer patients infected with S. aureus. Clinical data of 214 cases with S. aureus infection, hospitalized in Tianjin Medical University Cancer Institute and Hospital (TMUCIH), from 2011 to 2015, were reviewed. They were divided into a death group and survival group. WHONET 5.6 software and SPSS19.0 were used to analyze data. In the survival group, there were 83 male cases and 105 female cases, with a mean age of 55.9 ± 16.3 years old. In the death group, there were 15 male cases and 11 female cases, with a mean age of 52.9 ± 16 years old. Tumors in the digestive system of the two groups accounted for 36.2% and 30.8%, respectively. Main specimen types were blood (36.4%) and drainage fluid (49.1%). Bloodstream infections, no surgery, hospitalization of more than 2 times, with distant metastasis, without drainage tubes, and radiotherapy were potential prognostic risk factors in cancer patients with S. aureus infection ($P<0.05$). Logistic regression analysis showed that no surgery (OR = 0.261, 95% CI = 0.076-0.891, p = 0.032) and radiotherapy (OR = 4.796, 95% CI = 1.192-19.291, p = 0.027) were independent prognostic risk factors. These are necessary treatment means for cancer patients. However, the results of this study provide evidence helping clinicians prevent trouble before it happens, adopting comprehensive prevention and control measures, improving the prognosis of patients, and reducing mortality rates of S. aureus infection. The Methicillin-resistant Staphylococcus aureus (MRSA) ratio of S. aureus was 14.5%. No vancomycin, linezolid, and tigecycline resistant strains were detected.

Keywords: Cancer patients, staphylococcus aureus, infection, prognosis analysis

Introduction

Staphylococcus aureus (S. aureus) is one of the major pathogens in community and hospital-acquired bloodstream infections [1, 2]. The development of resistance to multiple drugs, including glycopeptides, has caused substantial difficulty in the management of S. aureus infections, which has been a worldwide concern [3, 4]. S. aureus infection incidence may be increasing, at least in some regions [5-7], probably due to higher numbers of invasive procedures and/or at-risk situations. Due to surgery, long-term stay intravenous catheters, repeated radiotherapy, and chemotherapy, cancer patients that suffer from inhibited bone marrow function, neutropenia, and mucosal barrier damage can be easily infected with Gram-positive bacteria [8, 9].

However, few studies have reported the prognostic factors of cancer patients infected with S. aureus. Such analysis can provide clinicians with evidence to help patients get better outcomes. This is of great significance. This study was conducted to investigate clinical characteristics of cancer patients with S. aureus infections in Tianjin Medical University Cancer Institute and Hospital (TMUCIH).

Table 1. Tumor types in patients with S. aureus infection

Tumor type	Survival group	Ratio (%)	Death group	Ratio (%)
Genitourinary tumor	20	10.6	5	19.2
Lung cancer	13	6.9	4	15.4
Pancreatic cancer	6	3.2	3	11.5
Nervous system tumors	4	2.1	3	11.5
Gastric cancer	22	11.7	1	3.8
Esophageal cancer	6	3.2	1	3.8
Breast cancer	39	20.7	1	3.8
Brain tumor	3	1.6	1	3.8
Lymphoma	10	5.3	1	3.8
Colorectal cancer	12	6.4	1	3.8
Liver cancer	13	6.9	1	3.8
Multiple myeloma	2	1.1	1	3.8
Cholangiocarcinoma	9	4.8	1	3.8
Sarcoma	9	4.8	0	0
Thyroid cancer	7	3.7	0	0
Other tumors	13	6.9	2	7.7
Total	188	100	26	100

Materials and methods

Ethics

This study was approved by the Research Ethics Committee of TMUCIH. Signed informed consent was obtained from all patients. All specimens were handled anonymously, according to ethical and legal standards.

Study design and data collection

This was a retrospective study to evaluate prognostic factors of S. aureus infection in patients with malignant tumors. Subjects included 214 cancer patients infected with S. aureus, from January 2011 to December 2015. In total, 188 patients were divided into the survival group and 26 patients into the death group. Clinical data including sex, age, tumor type, specimen type, Methicillin-resistant Staphylococcus aureus/Methicillin-sensitive Staphylococcus aureus (MRSA/MSSA), surgery, number of admissions, hospitalization days, distant organ metastasis of cancer, previous exposure to antibiotics, drainage tubes, central venous catheters, merger with other parts of infection, radiotherapy, chemotherapy, and mortality were collected.

Definitions

Hospital-acquired S. aureus infection was defined as the first positive culture obtained at 48 hours after hospital admission or 48 hours after discharge, along with clinical signs of active infection. Tumor types were confirmed by the pathologist. Pancreatic carcinoma, gastric carcinoma, esophageal carcinoma, colorectal carcinoma, hepatic carcinoma, and bile duct carcinoma were referred to as digestive system tumors. All clinical data were collected within 30 days prior to the first positive culture. Mortality referred to the ratio of death within 90 days after the first positive culture.

Bacterial identification and susceptibility tests

Blood samples (8-10 mL) or aseptic body fluids (5-10 mL) were collected and auto-cultured by BACTEC 9050, 9120, or FX400 (Becton-Dickinson, Franklin Lakes, NJ, USA) for 5 days. Positive samples were subcultured on blood agar (JinZhangKeJi, Tianjin, China) at 35°C for 24-48 hours depending on the results of gram staining. Species identification and bacterial susceptibility tests were performed on a VITEK 2 compact automatic microbiological analysis system (bio-Merieux SA, Marcy l'Etoile, France). All coincidence rates were above 95%.

Quality control

Control strains were S. aureus ATCC29213, Enterococcus faecalis ATCC 29212, and Streptococcus pneumoniae ATCC 49619.

Statistical analysis

WHONET 5.6 and SPSS19.0 software were used for statistical analysis. Data of categorical variables were compared by Fisher's exact test. Potential prognostic risk factors (p value <0.05) of S. aureus infection were included in the multivariate logistic regression model. P<0.05 indicates statistical significance. All tests were two-tailed.

Results

Clinical data of cancer patients with S. aureus infection

There were 15 males and 11 females in the death group, with an average age of 52.9 ± 16.0 years. The survival group consisted of 83

Table 2. Prognostic factors of cancer patients with S. aureus infection

Characteristics	Risk factors	Survival group (n = 188)	Death group (n = 26)	*p* value
Gender	Male	83 (44.1)	15 (57.7)	0.213
	Female	105 (55.9)	11 (42.3)	
Age	<60 years old	99 (52.7)	15 (57.7)	0.679
	≥ 60 years old	89 (47.3)	11 (42.3)	
Tumor type	Non-digestive system tumors	133 (70.7)	22 (84.6)	0.165
	Digestive system tumors	55 (29.3)	4 (15.4)	
Specimen type	Sterile body fluids	129 (68.6)	7 (26.9)	<0.001
	Blood	59 (31.4)	19 (73.1)	
MRSA	MRSA	25 (13.3)	2 (7.7)	0.543
	MSSA	163 (86.7)	24 (92.3)	
Surgery	Surgery	140 (74.5)	9 (34.6)	<0.001
	No surgery	48 (25.5)	17 (65.4)	
Number of admissions	≥ 2 times	78 (41.5)	19 (73.3)	0.003
	<2 times	110 (58.5)	7 (26.9)	
Hospitalization days	≥ 10 day	120 (63.8)	21 (80.8)	0.121
	<10 day	68 (36.2)	5 (19.2)	
Distant organ metastasis of cancer	Yes	79 (42.0)	17 (65.4)	0.034
	No	109 (58.0)	9 (34.6)	
Previous exposure to antibiotics	≥ 2 species	73 (38.8)	13 (50.0)	0.293
	<2 species	115 (61.2)	13 (50.0)	
Drainage tube	Yes	150 (79.8)	16 (61.5)	0.046
	No	38 (20.2)	10 (38.5)	
Central venous catheters	Yes	30 (16.0)	7 (26.9)	0.172
	No	158 (84.0)	19 (73.1)	
Merger with other parts of infection	Yes	137 (72.9)	16 (61.5)	0.250
	No	51 (27.1)	10 (38.5)	
Radiotherapy	Yes	7 (3.7)	7 (26.9)	<0.001
	No	181 (96.3)	19 (73.1)	
Chemotherapy	Yes	92 (48.9)	18 (69.2)	0.061
	No	96 (51.1)	8 (30.8)	

males and 105 females, with an average age of 55.9 ± 16.3 years. Types of malignant tumors are shown in **Table 1**, in which digestive system tumors of the survival group and death group accounted for 36.2% and 30.8%, respectively. S. aureus infection was found in various specimens, including 78 cases (36.4%) of blood, 105 cases (49.1%) of drainage fluid, 15 cases (7.0%) of catheters, and 8 cases (3.7%) of cerebrospinal fluid (0.9%).

Potential prognostic factors of cancer patients with S. aureus infection

Analysis of the 26 deaths and 188 survival patients found that bloodstream infections, no surgery, hospitalization ≥ 2 times, with distant organs metastases, no drainage tubes, and radiotherapy were potential prognostic risk factors for malignant tumor patients with S. aureus infection (P<0.05, **Table 2**).

Independent prognostic factors of cancer patients with S. aureus infection

Taking six potential risk factors into the multivariate Logistic regression model, results showed that no surgery and radiotherapy were independent prognostic factors for cancer patients with S. aureus infection (**Table 3**).

Drug resistance of S. aureus

MRSA ratio was 14.5%. Most antibiotic resistance of MRSA strains was significantly higher than the MSSA strains. No linezolid, vancomy-

Table 3. Regression analysis of prognostic factors of cancer patients with S. aureus infection

Risk factors	B	S.E.	Wald	*p* value	OR	95% CI
Specimen type	0.945	0.58	2.652	0.103	2.573	0.825-8.022
Number of admissions	0.531	0.586	0.822	0.365	1.7	0.540-5.357
Distant organ metastasis of cancer	0.273	0.501	0.296	0.586	1.314	0.492-3.509
Radiotherapy	1.568	0.71	4.874	0.027	4.796	1.192-19.291
Surgery	-1.345	0.627	4.597	0.032	0.261	0.076-0.891
Drainage tube	0.383	0.564	0.461	0.497	1.466	0.486-4.425

Table 4. Drug resistance analysis of S. aureus in patients with cancer

Antibiotic	Resistance rate (%)		*p* value
	MRSA (n = 27)	MSSA (n = 187)	
β-lactamase	100	80.2	<0.001
Penicillin	100	80.2	<0.001
Oxacillin	100	0	<0.001
Gentamicin	51.8	21.9	<0.001
Rifampin	29.6	0	<0.001
Ciprofloxacin	63	9.1	<0.001
Levofloxacin	63	9.1	<0.001
Moxifloxacin	55.6	8.6	<0.001
Cotrimoxazole	37	33.2	0.573
Clindamycin	59.3	30.5	<0.001
Erythromycin	85.2	54.5	<0.001
Linezolid	0	0	-
Vancomycin	0	0	-
Quinuptine/darfupin	0	0	-
Tetracycline	48.1	12.3	<0.001
Tigecycline	0	0	-

cin, and tigecycline-resistant S. aureus were detected. Mean MIC of vancomycin was 0.728, as shown in **Table 4**.

Discussion

S. aureus is an important opportunistic pathogen of nosocomial infections, widely colonized in human skin and medical devices. Infections caused by S. aureus are of poor prognosis and high mortality, leading to close examination by researchers [10-12]. In addition, cancer patients often undergo surgery, blood transfusions, radiotherapy, chemotherapy, indwelling catheters, and drainage tubes, increasing risks of S. aureus infection [13-15]. Therefore, this study retrospectively analyzed clinical data of 214 patients with S. aureus infection from January 2011 to December 2015.

In this study, the death rate of malignant tumor patients with S. aureus infection was 12.5%, slightly lower than one study reported [16, 17]. Patients with pancreatic cancer, stomach cancer, colorectal cancer, liver cancer, cholangiocarcinoma, and other digestive system cancers accounted for more than 30% of S. aureus infections. These patients often required abdominal surgery. S. aureus can colonize in the skin, surgical instruments, and intraperitoneal space. However, analysis showed that the relationship between type of tumor and prognosis of S. aureus infection was not significant ($P>0.05$).

Specimens of cancer patients infected with S. aureus were mainly blood and drainage fluid, accounting for 36.4% and 49.1% respectively. Statistical analysis showed that the mortality rate of bloodstream infection was significantly higher than that of other sterile liquids ($P< 0.001$). In addition, no surgery, hospitalization ≥ 2 times, with distant organs metastases, no drainage tubes, and radiotherapy were also potential prognostic risk factors for patients with S. aureus infections. However, multivariate logistic regression analysis showed that only no surgery and radiotherapy were independent prognostic risk factors ($P<0.05$). Weiser et al. and Tadroset et al. [18, 19] reported that surgery is one of the risk factors for S. aureus infection. Interestingly, in this study, surgery was a protective factor in the prognosis of cancer patients infected with S. aureus, possibly related to the fact that no surgical patients with distant organs metastases (58.8%) and radiotherapy (29.4%) were higher in the death group than those in the survival group (50%, 8.2%), but the differences were not statistically significant ($P>0.05$). Hayneset et al. and Loh et al. reported [20, 21] that radiation during radiotherapy can cause direct mucosal damage leading to apoptosis of epithelial cells and radiation due to the release of inflammatory media-

tors weakens the protective effects of the immune system. At the same time, radiation-induced neutrophils cell reduction also makes bacterial invasion easier, leading to infection. In this study, radiotherapy was an independent risk factor for prognosis of patients with malignant tumors infected with S. aureus.

In addition, the proportion of MRSA in patients with malignant tumors was 14.5%, lower than one study reported [22]. Drug resistance of MRSA to most antibiotics was higher than that of MSSA, indicating that it was more difficult to treat MRSA. However, there were no significant differences in prognosis ($P>0.05$). Mahajan et al. [9] reported that vancomycin MIC value ≥ 2 μg/mL is an independent risk factor for MRSA infection prognosis. The average vancomycin MIC in this study was 0.728, which was at a low level, consistent with a report from Holland et al. [23]. Vancomycin is still the first choice for treatment of MRSA.

In summary, absence of surgery and radiotherapy are independent risk factors for prognosis of cancer patients infected with S. aureus. However, both are indispensable means for patient treatment. Results of this present research provide evidence for clinicians to take precautionary and comprehensive measures, improving patient prognosis and reducing mortality rates of S. aureus infection.

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Disclosure of conflict of interest

None.

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