1069 Predictive Factors for Metastatic Infection in Patients with Bacteremia Caused by *Staphylococcus aureus*

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Submitted abstract

Background:
Metastatic infections, such as infective endocarditis and pyogenic spondylitis, are very serious complications of *Staphylococcus aureus* bacteremia (SAB), because failure to identify metastatic infections may cause poor prognosis. The aim of the present study is to determine the predictive factors for metastatic infections of SAB.

Methods:
This retrospective cohort study was conducted among patients with bacteremia due to *S. aureus* (including both methicillin-sensitive *S. aureus* and methicillin-resistant *S. aureus*: MSSA and MRSA) in The Jikei University Kashiwa Hospital. The study population comprised 125 adult patients with SAB between January 2014 and December 2017. Patients were excluded from this study for the following reasons: death or transfer to other hospital within 3 months after the initial positive blood culture was obtained. We analyzed several factors, including demographics, comorbidities, community acquisition, primary focus, persistent fever and laboratory data such as c-reactive protein (CRP) levels after treatment.

Results:
During the 4 years study period, 74 patients met inclusion criteria of this study. The most common primary site of bacteremia was catheter-related [24 (32.4 %) of 74]. Metastatic infection occurred in 22 (29.7 %) of 74 patients, and spondylitis was most common, following psoas abscess. Of these, 11 infections (50% of 22) were community acquired. We did not find any significant differences in demographics and comorbidities, except central venous catheter-associated bloodstream infection, which was associated with low rate of metastatic infection. By multivariate analysis, the predictive factors associated with the development of metastatic infection were community onset of infection (OR 11.6; 95% CI 2.98-45.1; *P*<0.001), persistent fever over 72 hours (OR 6.7; 95% CI 2.12-21.8; *P*=0.001), and higher CRP levels (>3mg/dl) lasting 2 weeks after the administration of appropriate antibiotics (OR 7.47; 95% CI 2.39-23.3; *P*<0.001).

Conclusion:
This study demonstrated that additional diagnostic tests to identify metastatic infection should be performed, especially in the patients with community-acquired SAB, persistent fever or persistently high CRP levels after the administration of appropriate antibiotics.

Background

- *Staphylococcus aureus* bacteremia (SAB) is the second most frequent cause of nosocomial bloodstream infection and can cause metastatic infections.

- Metastatic infections, such as infective endocarditis and pyogenic spondylitis are very serious complication of SAB, because failure to identify may result in bacteremia relapse and poor prognosis.

- Long term administration of antibiotics is necessary for patients with metastatic infections.

- We have previously determined that treatment delay and persistent fever or persistently high CRP levels after appropriate treatment are predictive factors for metastatic infection in MSSA bacteremia[1].

- In the present study, we aimed to clarify the predictive factors for metastatic infection in SAB (both MSSA and MRSA bacteremia) in order to administer antibiotics for appropriate period, so as not to fail treatment.

Methods

Definitions

- Metastatic infection was defined as deep seated infection detected within 3 months after the initial positive blood culture result was obtained.

- Community-acquired infection refers to infection in a patient who has had no recent contact with the health care system and a positive blood culture developed within 48 hours after hospital admission.

Methods

Patients

A retrospective cohort study of all SAB cases in adults ≧20 years old in The Jikei University Kashiwa Hospital from January 1 2014 to December 31 2017 was performed.

125 cases of *S.aureus* positive blood cultures reported by the bacterial laboratory

51 cases excluded
3 patients with repeat positive cultures
21 patients were transferred to another hospitals wihtin 90 days
27 patients died within 90 days

74 cases included in analysis

Statistical methods

Fisher's exact test was used to compare categorical variables. Student's t test was used to compare continuous variables. To determine the independent predictive factors for metastatic infections, a multiple logistic regression model was used to control the effects of confounding variables. All statistical analyses were performed with EZR [2] , which is a graphical user interface for R [3]. More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics.

Results

Table 1. localization of metastatic infections

Localization	Number of patients
Total number of patients	74
Absent	52(70.3%)
Present	22(29.7%)
Psoas abscess	5
Endocarditis	2
Lung	2
Spondylodiscitis	13
Epidural abscess	1
Joint	2
Vascular infection	2
Total number of metastatic infections	27

Table 1. Metastatic infection occurred in 22 of 74 patients (29.7 %), as follows: Psoas abscess 5, infective endocarditis 2, septic pulmonary abscess 2, spondylodiscitis 13, epidural abscess 1, septic arthritis 2, mycotic aneurysm 2.

Results

Table 2. Clinical characteristics of patients with SAB

	Metastatic infection		
	Present n=22	Absent n=52	*P*
Age, median (range)	71.5 (41-90)	70 (22-85)	0.933
Male gender, n (%)	17(77.3)	35(67.3)	0.285
Underlying disease, n (%)			
Leukemia	3(13.6)	4(7.7)	0.343
Malignant lymphoma	1(4.5)	5(9.6)	0.416
Solid tumor	3(13.6)	12(23.1)	0.279
Diabetic mellitus	6(27.3)	16(30.8)	0.497
Chronic kidney disease	5(22.7)	14(26.9)	0.476
Liver cirrhosis	2(9.1)	5(9.6)	0.657
Shock (systolic blood pressure < 90 mm Hg)	0(0)	5(9.6)	0.161
Community-acquired, n (%)	11(50)	5(9.6)	<0.001
Medication, n (%)			
Steroid	2(9.1)	11(21.2)	0.183
Immunosuppressive agent	4(18.2)	14(26.9)	0.313
Laboratory data at onset, n (%)			
Neutropenia (<500/mL)	1(4.5)	6(11.5)	0.323
Thrombocytopenia(<100,000/mL)	8(36.4)	11(21.2)	0.141
Hypoalbuminemia(<3g/dL)	14(63.6)	26(50)	0.318
MSSA bacteremia	16(72.7)	32(61.5)	0.259

Table 2. We demonstrated the relationship between clinical characteristics and metastatic infection. Univariate analysis revealed that community acquisition was determined to be the underlying factor associated with metastatic infection.

Table 3. Primary site of SAB

	Metastatic infection		
	Present n=22 n (%)	Absent n=52 n (%)	*P*
Primary site of infection			
Intravascular catheter	2 (9.1)	22 (42.3)	0.006
Central venous catheter	2 (9.1)	19 (36.5)	0.023
Skin and soft tissue infection	4 (18.2)	14 (26.9)	0.558
Respiratory tract	1 (4.5)	2 (3.8)	1
Urinary tract	1 (4.5)	7 (13.5)	0.422
intra-abdominal infection	0 (0)	1 (1.9)	1
unknown	14 (63.6)	6 (11.5)	<0.001

Table 3. The most common portal of entry was the catheter-associated (32.4%, 24/74), followed by skin and soft tissue infection (24.3%, 18/74). We found that catheter-associated bloodstream infection was associated with low risk for metastatic infection.

Results

Table 4. Antibiotic treatment and outcome

	Metastatic infection		
	Present n=22 n (%)	Absent n=52 n (%)	*P*
Treatment delay >48 hours	4(18.2)	9(17.3)	0.584
Persistent fever >72 hours	12(54.5)	9(17.3)	0.002
CRP >3.0 mg/dL lasting 2 weeks after treatment	14(63.6)	10(19.0)	<0.001

Table 4. Appropriate antimicrobial treatment was administered to 61 patients within 48 hours of SAB onset. Unlike previous study, treatment delay was not associated with metastatic infection in this study. We have to determine whether or not to continue antibiotics within 2 weeks after starting treatment, because at least 2 weeks of antimicrobial treatment is recommended for patients with uncomplicated SAB. Therefore, we investigated the lowest CRP levels during 2 weeks after onset of SAB. Consequently, we showed that the lowest CRP levels in patients with metastatic infection were significantly higher compared with those in patients without metastatic infection

Table 5. Predictive factors of the metastatic infection due to SAB in the logistic regression analysis

	OR	95% CI	*P*
Community-acquired	11.6	2.98-45.1	<0.001
Persistent fever > 72 hours	6.7	2.12-21.8	0.001
CRP > 3.0mg/dL lasting 2 weeks after treatment	7.47	2.39-23.3	<0.001

Table 5. The results of univariate analysis revealed that community-acquired bacteremia, persistent fever >72 hr, and CRP >3 mg/dL lasting 2 weeks after treatment were significant variables in relation to metastatic infection. Multivariate analysis was performed using shock status and immunosuppressive agent use as confounding variables. As a result, independent predictive factors for metastatic infection were determined to be community-acquired bacteremia, persistent fever >72hr and CRP > 3mg/dL lasting 2 weeks after treatment.

Conclusion

This study demonstrated that additional diagnostic tests to identify metastatic infection should be performed especially in the following patients.
Patients with：
· community-acquired *Staphylococcus aureus* bacteremia
· persistent fever or persistently high CRP levels after the administration of appropriate antibiotics.

References
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