Clinical Characteristics of *Staphylococcus aureus* Bacteremia with the Skip Phenomenon: a Case Control Study

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Background

➤ *Staphylococcus aureus* bacteremia (SAB) is one of the most common causes of persistent bacteremia, which is associated with complicated disease and poor clinical outcome.

➤ "The skip phenomenon (SP)" was recently proposed concept which might exhibit fluctuating blood culture positivity, but its clinical significance remained to be clarified.

Aim of the study

➤ To evaluate the clinical characteristics of SAB with the SP.

Method

➤ **Study design:** a retrospective case-control study, conducted at Kyoto University Hospital (1141-bed) during 2006-2021, was approved by the Ethics Committee of Kyoto University Graduate School and the Faculty of Medicine (R3240).

➤ **Participants:** adult inpatients with more than 3 days of SAB

➤ **Skip phenomenon:** at least 1 day of negative blood cultures following documented SAB and preceding recurrence of a positive blood culture, which was taken within 14 days from last positive culture.

➤ **Cases/controls:** cases were patients with SP, and controls were the rest of the patients.

➤ **Duration of bacteremia:** counted from the day of collection of the first positive culture to the day of collection of the last positive culture.

Results

➤ Of the 173 patients, 17 (9.8 %) had the SP (Figure 1).

➤ A total of 20 SP episodes among 17 cases were observed. Three patients had 2 episodes of SP.

➤ Of the 20 episodes of the SP, 7 (35.0 %) were confirmed with single set, and 13 (65.0 %) were confirmed with 2 sets of negative blood culture.

➤ The median interval from first positive blood culture to first SP episode in each case was 7 days (interquartile range [IQR], 6-16 days).

Table. Patient characteristics.

	SP (n=17) N, %		Control (n=156) N, %		P-value
Age	71	54-77	69	51.75-77	0.192
Male	10	58.8	90	57.7	1.000
Duration of bacteremia	14	12-33	4	4-6	<0.001
Charleson comorbidity index	3	2-4	2	1-4	0.279
SOFA score	3	1-4	4	1-6	0.338
Methicillin resistant	13	76.5	83	53.2	0.077
Site of onset					0.604
Community-onset	4	23.5	30	19.2	
Healthcare-associated	1	5.9	25	16.0	
Nosocomial	12	70.6	101	64.7	
Medical comorbidities					
Active malignancy	3	17.6	44	28.2	0.566
Transplant	1	5.9	12	7.7	1.000
Connective tissue disease	1	5.9	20	12.8	0.698
Chronic immunosuppresive therapy	3	17.6	45	28.8	0.405
Chronic skin condition	1	5.9	23	14.7	0.473
Diabetes mellitus	9	52.9	39	25.0	0.022
Hemodialysis	2	11.8	28	17.9	0.740
Liver disease/cirrhosis	2	11.8	25	16.0	1.000
Tobacco use	2	11.8	8	5.1	0.260
Implanted hardware					
CIED	2	11.8	10	6.4	0.334
CVC	5	29.4	65	41.7	0.438
Prosthetic joint	1	5.9	5	3.2	0.468
Prosthetic valve	2	11.8	8	5.1	0.256
Prosthetic vascular graft	1	5.9	6	3.8	0.522
Focus of infection					
IE	4	23.5	20	12.8	0.262
Osteomyelitis	5	29.4	25	16.0	0.180
Deep-seated abscess	4	23.5	28	17.9	0.524
Arthritis	2	11.8	12	7.7	0.632
CRBSI	7	41.2	63	40.4	1.000
Unknown	1	5.9	27	17.3	0.314
Respiratory	0	0.0	8	5.1	1.000
Prognosis					
30-day mortality	0	0.0	29	18.6	0.080
90-day mortality	3	17.6	43	27.6	0.565
In-hospital mortality	3	17.6	39	25.0	0.766

SOFA, sequential organ failure assessment. CIED, cardiac implantable electric device. CVC, central venous catheter. IE, infective endocarditis. CRBSI, catheter-related bloodstream infection. SP, skip phenomenon.

Figure. Swimmer plot of the patients with the skip phenomenon.

Patients with the skip phenomenon

■ Duration of bacteremia　● Negative blood culture　▲ Positive blood culture
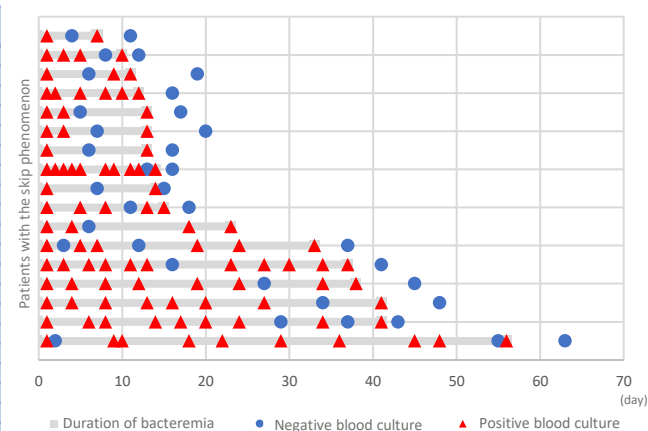
➤ Of 20 episodes of SP, 18 (90.0 %) were accompanied with fever as an indication for taking blood culture.

➤ The cases (n=17) were more likely than controls (n=132) to have a longer duration of bacteremia (median [IQR], 14 [11–36] days, vs 4 [3–7] days; p<0.001), and diabetes mellitus (52.9 % vs 25.0 %, p=0.022) (table 1).

➤ There was no significant difference in deep-seated infection* (64.7 % vs 48.5 %, p=0.303), methicillin resistance rate (76.5 % vs 50.0 %, p=0.068), and 90-day mortality (17.6 % vs 27.3 %, p=0.561) between cases and controls.

＊ Infective endocarditis, osteomyelitis, and deep-seated abscess.

Conclusion

➤ Our findings suggest that we should consider to take blood culture repeatedly when clinically indicated (e.g. fever, elevation of inflammatory marker), even if we confirmed the negative once before.

Disclosure of conflict of interest: none.