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Clinical Impact of Bacteremia Due to *Staphylococcus saprophyticus*

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Abstract

Objective: This was a retrospective study to evaluate the clinical impact of bacteremia due to *Staphylococcus saprophyticus* and identify which factors influence it. **Methods:** We reviewed all patients with bacteremia due to *S. saprophyticus* over the last 12 years. This study was performed at Jichi Medical University Hospital in Japan, a key hospital in the northern Kanto area including Tochigi, Gunma, Ibagagi, and northern Saitama prefectures. We retrospectively reviewed the blood culture results and medical records of all patients with a history of visits or hospitalizations between April 2008 and September 2020. **Results:** During the study period, 4 blood culture specimens were considered to have *S. saprophyticus* bacteremia. Two of these were from subjects > 60 years old who had severe infection. A third case, 27 years old, was thought to have a catheter-related bloodstream infection; however, the only symptom was fever, which was not serious. The fourth case, a previously unreported pediatric patient, had non-severe fever. The mean time for a diagnosis of bacteremia by blood culture testing was 42 hours, whereas contamination appeared in cultures after another 50 hours. **Conclusion:** The pathogenicity of *S. saprophyticus* might be lower in the blood than in the urine due to its physiological function and activity. In older adults with underlying diseases, the severity of bacteremia was more pronounced, whereas in a young adult and a child, the disease was relatively mild. Age and underlying disease might be useful factors to consider when diagnosing bacteremia due to *S. saprophyticus*.

Keywords

Gram-Positive *Staphylococcus*, Coagulase-Negative *Staphylococcus*,

Staphylococcus saprophyticus, Bacteremia

1. Introduction

Staphylococcus saprophyticus, a Gram-positive, novobiocin-resistant, coagulase-negative *Staphylococcus*, is a frequent causative microorganism of acute urinary tract infections in women, accounting for up to 42.3% of such infections in women aged 16 - 25 years [1]. The gastrointestinal tract is a major reservoir of *S. saprophyticus* and the strain was reported to be isolated from urogenital tract specimens collected from 6.9% of healthy women, with the most common site of colonization being the rectum (40%) [2]. However, the clinical significance of this organism isolated from blood cultures has not been well defined. To date, only a few cases of *S. saprophyticus* bacteremia including endocarditis have been reported [3] [4] [5] [6] [7]. The clinical impact of bacteremia caused by *S. saprophyticus* in patients without indwelling medical devices or in patients who are not immunosuppressed is unclear.

Here, we report accumulated cases of bacteremia related to *S. saprophyticus* and retrospectively evaluate the patient's background and the clinical virulence among patients who developed bacteremia due to *S. saprophyticus* as determined from the data of patients diagnosed in our hospital. There have been no previously reported cases in children under 10 years of age. We also report on the diagnosis and treatment of pediatric cases we have been involved in. This study was approved by the ethics committee of our hospital (approval number: 20-098).

2. Case Results

This study was performed at Jichi Medical University Hospital in Japan, a key hospital providing high quality advanced acute and acute care in the northern Kanto area including Tochigi, Gunma, Ibagagi, and northern Saitama prefectures. The hospital currently has 1132 beds and 46 clinical sections. In 2019, there were approximately 337,000 inpatients, 626,000 outpatients, and 9700 surgeries performed.

We retrospectively reviewed the blood culture results and medical records of all patients with a history of visits or hospitalizations between April 2008 and September 2020. All blood cultures were processed by the hospital microbiology laboratory using a standard blood culturing system (BACTEC FX; Becton Dickinson and Company). Antibiotic susceptibilities were determined using a VITEK 2 (bioMerieux, Inc.) system using standard criteria prescribed by the Clinical Laboratory Standards Institute. *S. saprophyticus* blood isolates were considered significant if 2 separate blood cultures were positive (in children, even a single positive blood culture was considered significant) and if systemic inflammatory response syndrome was present without any alternate explanation; that is, pa-

tients had to have had at least 2 or more of the following 4 criteria: 1) body temperature of >38˚C or <36˚C, 2) heart rate of > 90 beats per minute, 3) respiratory rate of >20 breaths per minute, and 4) peripheral white blood cell count of >12,000/mm^3 or <4000/mm^3 or the presence of >10% immature neutrophils ("bands") [8] [9].

During the study period, the number of positive blood culture specimens was 11,770 out of 128,730, of which 2542 were positive for coagulase-negative bacteria. Among these, 14 blood culture specimens from 13 patients were positive for *S. saprophyticus*. Of these 14 specimens, 4 specimens were considered to have clinically significant bacteremia, whereas the remaining 10 episodes were regarded as cases of contamination. These contaminated cases were considered related to not using the prescribed disinfection methods when blood culture samples were collected, feverless cases collected by routine preoperative examination, cases of intracranial hemorrhage but not brain abscess that resulted in unconsciousness and transportation to the emergency room, or cases of feverless convulsions during dialysis. These contaminant cases were not treated with antibiotics and their clinical course was uneventful.

The clinical and microbiologic characteristics of 4 patients with clinically significant *S. saprophyticus* bacteremia are shown in Table 1.

Case 1 (a 63-year-old male) was an outpatient who had hypothermia (32˚C) due to septic shock. Chronic pancreatitis and alcoholic liver disease were his underlying diseases, but he was taking no medication other than for hyperlipidemia. He

Table 1. Clinical characteristics of *S. saprophyticus* bacteremia patients.

Case no.	Sex/ Age (y)	Reason for admission/ sample collection	Underlying clinical factors	Probable source of bacteremia	Urine culture	Resistance antibiotics	Concomitant blood isolate	Therapy	Outcome
1	M/63	Septic shock	Chronic pancreatitis, Alcoholic liver disease, Hyperlipidemia	Acute pyelonephritis	Antibiotic treatment started before urine culture, urine culture is negative	PCG, EM, CLDM, FOM, LVFX	-	Vancomycin	Recovered
2	M/86	Acute prostatitis	Chronic pancreatitis, Hypertension	Acute prostatitis	Antibiotic treatment started before urine culture, urine culture is negative	PCG, FOM	-	Vancomycin	Recovered
3	F/27	Fever during bronchial asthma treatment	Bronchial asthma	Central venous catheter	Negative	1) PIPC, PCG, CEZ, EM, CLDM, FOM 2) PCG, EM, CLDM	Two *S. saprophyticus* strains with different drug sensitivities	Vancomycin	Recovered
4	F/8	Fever without any other symptoms	Rheumatic fever	Unknown	Negative	PIPC, PCG, CEZ, EM, CLDM, FOM	-	Vancomycin	Recovered

PCG, Penicillin G; PIPC, Piperacillin; CEZ, Cefazolin; EM, Erythromycin; CLDM, Clindamycin; FOM, Fosfomycin; LVFX, Levofloxacin.

was in a poor state of consciousness and was promptly started on warming and respiratory and cardiovascular management. Based on vital signs indicating shock, urine and blood analysis results, and septic shock, urinary tract infection was suspected as a focus, and meropenem and vancomycin were selected based on the patient's underlying medical condition and history of previous hospitalization. Multiple organ failure due to hypothermia became more pronounced, but he recovered 1 month after treatment.

Case 2 (an 86-year-old male) was an outpatient who had a high fever of 38.2˚C. Chronic pancreatitis and hypertension were his underlying diseases, but he was not receiving any medication. The patient was admitted to the hospital for treatment due to a deterioration of his general condition and reduced level of consciousness with high-grade fever. Clinical analysis indicated severe infection. Based on his clinical symptoms and fever focus work-up including blood and urine analysis, he was diagnosed with acute prostatitis prior to the onset of bacteremia. After admission, piperacillin-tazobactam was chosen as the initial antibiotic treatment; however, after bacteremia caused by *S. saprophyticus* was identified and the patient had a persistent low-grade fever, antibiotics were changed to vancomycin based on drug sensitivity, and he completed the treatment without any complications.

Case 3 (a 27-year-old female) was the only patient who received immunosuppressive drugs for 2 months to treat a major bronchial asthma attack. A central venous catheter was inserted 3 weeks before the fever onset because the asthma treatment was expected to be prolonged. At fever onset, there was no redness or swelling of the skin at the catheter insertion site and no exacerbation of bronchial asthma or other clinical symptoms. Various culture tests, including urine, did not detect any suspected infectious organisms. Blood cultures taken from the catheter confirmed bacteremia. Cefazolin and vancomycin were selected based on the patient's underlying medical condition and history of previous hospitalization.

She followed a slightly different clinical course from the other cases. At the time of bacteremia diagnosis, 2 different *S. saprophyticus* strains were detected. Blood culture 5 days after the start of antibiotic treatment was negative. Three months later, during a close examination of fever without any other symptoms that occurred during a bronchial asthma flare-up, a blood culture taken from a catheter tested positive for *S. saprophyticus*. *S. saprophyticus* had comparable drug sensitivity to 1 of the 2 *S. saprophyticus* strains detected 3 months earlier. Due to re-infection, the catheter was promptly removed and she was re-treated with vancomycin and recovered quickly.

Case 4 (an 8-year-old female), was an outpatient pediatric case with a high-grade fever of 39˚C without any other symptoms, and her general condition had been good for 4 days. She had a history of rheumatic fever and was treated with oral penicillin as prophylaxis for streptococcal infection and aspirin as an anti-inflammatory agent for half a year. No urinary tract infection or inserted vascular device was identified before admission. Various urine, vaginal,

and rectal cultures were performed; however, no *S. saprophyticus* was detected except in the blood. The source and the route of infection were not clear. After admission, ceftriaxone was selected, but was changed to vancomycin because of the detection of *S. saprophyticus*. She responded well to vancomycin and completed treatment without any complications.

S. saprophyticus was diagnosed as bacteremia within 48 hours of starting blood cultures, with a mean of 42 hours, whereas the 10 cases that tested positive for contamination were positive at 72 to 120 hours after starting blood culture, with a mean of 92 hours. The drug sensitivity testing showed that only case 4 was resistant to methicillin. Repeated blood cultures were performed for all patients at 3 to 7 days after starting vancomycin. All cases were treated with vancomycin for 7 to 14 days. Follow-up for over 3 years after treatment demonstrated no recurrence of bacteremia including *S. saprophyticus* in all cases.

3. Discussion

S. saprophyticus bacteremia has rarely been reported [3] [4] [5] [6] [7]. A few cases of *S. saprophyticus* bacteremia from a urinary tract infection were identified [3], and most *S. saprophyticus* bacteremia cases were associated with catheter-related infections [5] [6]. When *S. saprophyticus* is isolated in a blood culture, as with other coagulase-negative bacteria, it is often considered to be a case of contamination due to its low pathogenicity. *S. saprophyticus* does not possess a potassium acquisition system such as ATPase, which is necessary for bacterial growth [10]. The concentration of potassium in urine is 8 - 12 times higher than that in the plasma [11]. In addition to cell-wall associated proteins, urease and d-serine deaminase activities are considered crucial for efficient colonization and pathogenicity in urinary tract infection, but not for blood infection [12]. One reason for this might be that *S. saprophyticus* does not produce coagulase, which is resistant to phagocytosis by producing blood clots and coating the bacterial surface [5]. Therefore, even if *S. saprophyticus* enters the bloodstream, it is unlikely to cause the same pathogenicity as in urinary tissues due to its physiological function and activity. In support of this speculation, the general condition of our pediatric case did not deteriorate. There are no previous reports of bacteremia caused by *S. saprophyticus* in children less than 10 years old (the youngest was 14 years old [5]); therefore, the clinical picture of this disease is still unclear. However, our findings suggest that pediatric cases might have a less severe clinical course than that in adults. Indeed, in this study, 2 adult cases of bacteremia were severe, suggesting that factors such as age, underlying diseases, or infections triggered by bacteremia may be involved in the severity of the disease.

It is difficult to confirm coagulase-negative bacteria as a causative agent of bacteremia because of the high number of detections in blood culture tests and because it is an indigenous bacterium of the skin that easily causes contamination. Therefore, various perspectives are needed to make an accurate diagnosis. One of the determining factors is the time it takes for the bacteria to become

positive after the start of culture. In general, a positive test early after the start of culture is thought to reflect bacteremia. For blood culture tests, an approximately 5-fold or greater difference in the number of bacteria in blood samples was reported between bacteremia and contamination [8].

The early detection of bacteria after the start of a culture test is highly indicative of bacteremia [13] [14] [15]. In our study, cases of bacteremia were diagnosed as positive 42 hours after the start of culture testing, which is about 50 hours earlier than that caused by contamination. Even in cases of slow-growing *S. saprophyticus*, the time from the start of the test to positive confirmation of an organism in the blood suggests that it can distinguish between contamination and bacteremia.

This study had some limitations. First, the number of eligible cases was small. Because there were 3 adult cases and 1 pediatric case, we might not have captured the exact clinical presentation trends of *S. saprophyticus* bacteremia. Second, this study was retrospective, which might have led to reporting bias and poor quality of medical record data. Furthermore, we did not perform a molecular biological evaluation of the detected *S. saprophyticus*.

4. Summary

In summary, 4 cases of bacteremia due to *S. saprophyticus* were presented: 3 were adult cases, 2 of which we considered to have developed severe bacteremia from urinary tract infection due to *S. saprophyticus*. The other case was due to long-term central venous catheter infection; however, this was not severe. One case was a child and their infection was also not severe. The route of infection was unknown. We speculate that the risk of severe *S. saprophyticus* bacteremia may vary depending on underlying disease, age, and the infection that triggers bacteremia.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Wallmark, G., Arremark, I. and Ternhag, A. (1978) *Staphylococcus saprophyticus*: A Frequrtent Cause of Acute Urinary Tract Infection among Female Outpatients. *The Journal of Infectious Diseases*, **138**, 791-797. https://doi.org/10.1093/infdis/138.6.791

[2] Rupp, M.E., Soper, D.E. and Archer, G.L. (1992) Colonization of the Female Genital Tract with *Staphylococcus saprophyticus*. *Journal of Clinical Microbiology*, **30**, 2975-2979. https://doi.org/10.1128/JCM.30.11.2975-2979.1992

[3] Choi, S.-H., Woo, J.H., Jeong, J.-Y., Kim, N.J., Kim, M.-N., Kim, Y.S. and Ryu, J.

(2006) Clinical Significance of *Staphylosoccus saprophyticus* Identified on Blood Culture in a Tertiary Care Hospital. *Diagnostic Microbiology and Infectious Disease*, **56**, 337-339. https://doi.org/10.1016/j.diagmicrobio.2006.08.012

[4] Jame, P.N. and Joseph, W.S.G. (1988) Septicemia Caused by *Staphylococcus saprophyticus* without Associated Urinary Tract Infection. *The Pediatric Infectious Disease Journal*, **7**, 601-602. https://doi.org/10.1097/00006454-198808000-00004

[5] Hur, J., Lee, A., Jo, W.Y., Cho, O.H., Kim, S. and Bae, I.G. (2016) Staphylococccus Saprophyticus Bacteremia Originating from Urinary Tract Infections: A Case Report. *Infection & Chemotherapy*, **48**, 136-139. https://doi.org/10.3947/ic.2016.48.2.136

[6] Nishimura, S., Masuyama, S. and Yamamoto, K. (2020) *Staphylococccus saprophyticus* Native Endocarditis Possibly Originating from the Lower Gastrointestinal tract. *IDCases*, 19, e00713. https://doi.org/10.1016/j.idcr.2020.e00713

[7] Magarifuchi, H., Kusaba, K., Yamakuchi, H., Hamada, Y., Urakami, T. and Aoki, Y. (2015) *Staphylococcus saprophyticus* Native Valve Endocarditis in a Diabetic Patients with Neurogenic Bladder: A Case Report. *Journal of Infection and Chemotherapy*, **21**, 695-699. https://doi.org/10.1016/j.jiac.2015.05.008

[8] Herwaldt, L.A., Geiss, M., Kao, C. and Pfaller, M.A. (1996) The Positive Predictive Value of Isolating Coagulase-Negative Staphylococci from Blood Cultures. *Clinical Infectious Diseases*, **22**, 14-20. https://doi.org/10.1093/clinids/22.1.14

[9] Bone, R.C., Sibbald, W.J. and Sprung, C.L. (1992) The ACCP-SCCM Consensus Conference on Sepsis and Organ Failure. *Chest*, **101**, 1481-483. https://doi.org/10.1378/chest.101.6.1481

[10] Kuroda, M., Yamashita, A., Hirakawa, H., Kumano, M., Morikawa, K., Higashide, M., Maruyama, A., Inose, Y., Matoba, K., Toh, H., Kuhara, S., Hattori, M. and Ohta, T. (2005) Whole Geneme Sequence of *Staphylococccus saprophyticus* Reveals the Pathogenesis of Uncomplicated Urinary Tract Infection. *Proceedings of the National Academy of Sciences of the United States of America*, **102**, 13272-13277. https://doi.org/10.1073/pnas.0502950102

[11] Malhotra, M.S., Sridharan, K. and Venkataswamy, Y. (1976) Potassium Losses in Sweat under Heat Stress. *Aviation, Space, and Environmental Medicine*, **47**, 503-504.

[12] Weslley, P.S., Viviane, S.S. and Marcia, G.M. (2018) Occurrence of Virulence-Associated Genes among *Staphylococccus saprophyticus* Isolated from Difference Sources. *Microbial Pathogenesis*, **119**, 9-11. https://doi.org/10.1016/j.micpath.2018.03.054

[13] Osaki, S., Kikuchi, K., Moritoki, Y., Motegi, C., Ohyatsu, S., Nariyama, T., Matsumoto, K., Tsunashima, H., Kikuyama, T., Kubota, J., Nagumo, K., Fujioka, H., Kato, R. and Murakawa, Y. (2020) Distinguishing Coagulase-Negative Staphylococcus Bacteremia from Contamination Using Blood-Culture Positive Bottle Detection Pattern and Time to Positivity. *Journal of Infection and Chemotherapy*, **26**, 672-675. https://doi.org/10.1016/j.jiac.2020.02.004

[14] Kirchhoff, L.V. and Sheagren, J.N. (1985) Epidemiology and Clinical Significance of Blood Cultures Positive for Coagulase-Negative Staphylococcus. *Infection Control & Hospital Epidemiology*, **6**, 479-486. https://doi.org/10.1017/S0195941700063591

[15] Morioka, S., Ichikawa, M., Mori, K. and Kurai, H. (2018) Coagulase-Negative Staphylococcal Bacteraemia in Cancer Patients. Time to Positive Culture Can Distinguish Bacteraemia from Contamination. *Infectious Diseases*, **50**, 660-665. https://doi.org/10.1080/23744235.2018.1451917