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Original article

# Bloodstream infections caused by *Streptococcus anginosus* group bacteria: A retrospective analysis of 78 cases at a Japanese tertiary hospital

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ABSTRACT

*Objectives:* To investigate the characteristics of *Streptococcus anginosus* group (SAG) bacteremia in recent years, we conducted a retrospective cohort study and compared its findings with the data from previous studies.
*Methods:* All patients with positive blood cultures from May 2005 to September 2014 in a tertiary care center with 925 beds were included.
*Results:* There were 78 cases of SAG bacteremia (51 cases men; median age, 68 years) during the study period. The most common comorbidities were solid tumors in 32.1% of the patients. The most common infection source was hepatobiliary in one-third of all cases. Other infection sites included the following: intra-abdominal (12.8%), thoracic (10.3%), musculoskeletal (9%), urinary tract (7.7%), soft tissues (7.7%), and cervicofacial (6.4%). Susceptibility to penicillin, clindamycin and erythromycin were 100% (78/78), 95% (70/74) and 85% (39/46), respectively. Surgery along with systemic antibiotic treatment was administered in 53% of the cases. In-hospital mortality was 14.1%.
*Conclusion:* The clinical sources of the SAG bacteria were diverse, and hepatobiliary infection was the most common source of infection. In more than half of the patients, surgical treatment was performed. Susceptibility to penicillin was 100%, but susceptibility to erythromycin was lower than that reported in previous studies.


## 1. Introduction

*Streptococcus anginosus* group (SAG) bacteria, formerly referred to as the *Streptococcus milleri* group, consists of three distinct streptococcus species [1]: *S. anginosus*, *Streptococcus constellatus*, and *Streptococcus intermedius*. SAG bacteria, classified as viridans streptococci, have clinically distinct characteristics from other viridians streptococci in that they cause pyogenic infections in various parts of the body [2]. Bacteremia caused by this group is associated with infections that require surgical treatment [3]. To date, few studies have examined the clinical importance of SAG bacteremia, and most of these studies were conducted before 2000 [4–8]. To investigate the characteristics of SAG bacteremia in recent years, we conducted this retrospective cohort study and compared its findings with the data from previous studies.

## 2. Patients and methods

We reviewed the medical records of all patients who had SAG bacteremia in Kameda Medical Center, a tertiary care center with 925 beds in Kamogawa, Japan. We also compared the characteristics of the different species. This study was approved by the Committee for Ethics of Kameda Medical Center, Japan under the condition that personal data was kept confidential. Because of the

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retrospective, observational nature of the study, the requirement for informed consent was waived by the Committee.

All patients with positive blood cultures from May 2005 to September 2014 were screened using our laboratory database. SAG-positive blood cultures were identified and investigated using electronic medical records. If more than two blood cultures were positive for SAG, the patient was considered to have had true bacteremia. Also, cases where only one blood culture grew SAG and where the clinical judgement of plural infectious diseases expertise was consistent with SAG bacteremia, the cases were considered to be true bacteremia. If only one blood culture was positive and there was no other sign of sepsis, it was considered to be a result of contamination.

We gathered information on age, sex, number of positive blood cultures, underlying health conditions (solid tumor, lymphoma, leukemia, congestive heart failure, myocardial infarction, peripheral vascular disease, cerebrovascular disease, hemiplegia, dementia, chronic pulmonary condition, connective tissue diseases, peptic ulcer disease, diabetes mellitus, moderate to severe chronic kidney disease, liver disease and AIDs), vital signs on the day of the positive blood culture, source of infection, susceptibility of organism isolated to various antibiotics, choice and duration of antibiotic treatment, performance of surgical treatment and in-hospital mortality. We also calculated the Charlson Comorbidity Index (CCI) [9] using the information about the comorbidities. The source of infection was determined if SAG from another specimen grew or there was a clinically evident site of infection. If there was no clinically evident site of infection in a patient with true bacteremia, it was recorded as primary bacteremia. The severity of the bacteremia on the day of onset was graded by the Pitt Bacteremia Score (PBS) [10].

Blood specimens were processed in the microbiology laboratories using the BACTEC blood culture system (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). For blood culture bottles, we used BD BACTEC Plus Aerobic/F Culture Vials, BD BACTEC Lytic/10 Anaerobic/F Culture Vials and BD BACTEC Myco/F Lytic Culture Vials (Becton, Dickinson and Company). Bottles were incubated at 37 °C and examined daily for 7 days. Organisms were identified to the species level using the Microscan WalkAway system (Beckman Coulter, Miami, FL, USA) and the Rapid ID32 Strep system (bioMérieux, France). Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonics, Germany) was used to identify species that could not be classified by the Rapid ID32 Strep system. Broth microdilution methodology was used to determine the minimal inhibitory concentrations of the antibiotics that were tested. Isolate susceptibility to various antibiotics was judged according to Clinical and Laboratory Standards Institute (CLSI) M100-S24 [11].

**Table 1**
Summary of patient demographics, clinical characteristics, microbiological characteristics, treatment and outcomes.

| Variables | |
|---|---|
| Median age, years (IQR) (n = 78) | 67.4 (59.3–80.0) |
| Men, n (%) (n = 78) | 51 (65.4) |
| Comorbidities, n (%) (n = 78) | |
| Solid tumor | 25 (32.1) |
| Diabetes mellitus | 14 (18.0) |
| Heart failure | 10 (13.2) |
| Liver disease | 10 (12.8) |
| Dementia | 10 (12.8) |
| Hemiplegia | 9 (11.5) |
| Cerebral vascular disease | 9 (11.5) |
| Myocardial infarction | 6 (7.7) |
| Collagen disease | 5 (6.4) |
| Peripheral artery disease | 5 (6.4) |
| Chronic respiratory disease | 4 (5.1) |
| Peptic ulcer disease | 3 (3.9) |
| Chronic kidney disease | 3 (3.9) |
| Leukemia | 1 (1.3) |
| Lymphoma | 0 |
| AIDS | 0 |
| Charlson Comorbidity Index, n (%) (n = 78) | |
| 0 | 19 (24.4) |
| 1–2 | 24 (30.8) |
| 3–4 | 10 (12.8) |
| 5– | 25 (32.1) |
| Pitt Bacteremia Score, n (%) (n = 75) | |
| –4 | 68 (90.7) |
| 5– | 7 (9.3) |
| Source of infection, n (%) (n = 78) | |
| Hepatobiliary | 25 (32.1) |
| Intra-abdominal | 9 (11.5) |
| Thoracic | 8 (10.2) |
| Urinary tract | 6 (7.7) |
| Soft tissue | 6 (7.7) |
| Musculoskeletal | 5 (6.4) |
| Cervicofacial | 5 (6.4) |
| Infective endocarditis | 3 (3.8) |
| Central nervous system | 1 (1.3) |
| Primary bacteremia | 7 (9.0) |
| Multiple source of infection | 3 (3.8) |
| Polymicrobial bacteremia, n (%) (n = 78) | 28 (35.9) |
| Species, n (%) (n = 78) | |
| *S. constellatus* | 27 (34.6) |
| *S. intermedius* | 19 (24.4) |
| *S. anginosus* | 17 (21.8) |
| Not identified | 15 (19.2) |
| Susceptibility, susceptible/all (%) (n = 78) | |
| PCN | 78/78 (100) |
| CLDM | 70/74 (94.6) |
| EM | 39/46 (84.8) |
| Surgical treatment, n (%) (n = 78) | 41 (52.6) |
| Treatment duration, median days (IQR) (n = 78) | 19 (14–39) |
| In-hospital mortality, n (%) (n = 78) | 11 (14.1) |

## 3. Results

In total, 136 sets of blood cultures from 83 cases were SAG-positive. Of these, five cases were judged to be the result of contamination. Thus, there were 78 cases in total during the study period. Patient demographics, clinical characteristics, microbiological characteristics, therapy and outcomes are summarized in Table 1. The most common source of infection was hepatobiliary-related (32.1%). Multiple sources of infection were found in three cases (3.8%). One case had infective endocarditis (IE) complicated by vertebral osteomyelitis. Another case had sigmoid cancer with an intra-abdominal abscess extending to the spinal space, then complicated by bacterial meningitis. The last case had concomitant hepatic abscess and iliopsoas abscess. IE was seen in four cases; among these, two cases involved both the mitral and aortic valves. Two other cases involved the mitral valve alone and two cases required valve replacement. Central nervous system (CNS) infection was seen in two cases. One case had a brain abscess and the other had bacterial meningitis. Among the 71 cases whose sources of infection were found, the same organisms were identified as being from a local site in 30 cases (42.2%).

Polymicrobial bacteremia was seen in 28 cases (35.9%). Table 2 shows the microorganisms identified along with the SAG bacteria. Gastrointestinal flora was the most frequently identified group, followed by obligate anaerobes, skin and nasopharynx flora and oral flora. *S. constellatus*, *S. intermedius* and *S. anginosus* were identified in 27, 19 and 17 cases, respectively. In 15 cases, we could not identify the organism at the species level (reported as *S. milleri* group or SAG). Three cases of *S. anginosus* and one case of *S. constellatus* were identified by MALDI-TOF MS. Surgical treatment and systemic antibiotics were used in 53% of the cases. The