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Laboratory and epidemiology communications

Transient Bacteremia due to *Streptococcus gallolyticus* subsp. *pasteurianus* in a 3-year-old Infant

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*Streptococcus galloyticus* subsp. *pasteurianus* is a Lancefield group D streptococcus, formerly known as *Streptococcus bovis* biotype II/2 (1). Invasive diseases due to this organism have been reported mainly in elderly adults with variable clinical syndromes, including bacteremia, endocarditis, meningitis, osteomyelitis, peritonitis, and solid organ abscess (2, 3). In contrast, *S. galloyticus* subsp. *pasteurianus* infection is considered uncommon among children, and pediatric cases that have presented with either bacteremia or meningitis have been exclusively in those younger than 3 months of age (2-12). Here, we report the first case of *S. galloyticus* subsp. *pasteurianus* bacteremia in a much older infant, which was spontaneously resolved without any antimicrobial agents. Informed consent was obtained from the patient’s parents for publication. This case study was approved by the review board at Nishi-Kobe Medical Center.

A previously healthy 3-year-6-month-old boy presented to the Emergency Department at our hospital with a 1-day history of watery diarrhea, vomiting, and fever. His elder brother had developed rotavirus infection 3 days prior. At arrival, the vital signs included fever of 40°C and pulse rate of 150/min. The rest of the physical examination was unremarkable. The peripheral blood analysis included WBC of 7300/μL and C-reactive protein of 0.5 mg/dL. High fever led us to obtain blood culture in a bottle specialized for children (Peds plus/F, Becton, Dickinson and Company). With a positive rotavirus antigen test of the stool, the patient was diagnosed as having rotaviral gastroenterocolitis, and received fluid administration in the Emergency Department. At 11.8 hours after incubation, blood culture yielded growth of Gram-positive cocci, both catalase- and coagulase-negative. After the report of positive blood culture, the patient was requested to revisit our hospital. At the second referral on the next day, the patient had become afebrile without any treatment with antimicrobial agents. A follow-up evaluation at 10 days after the onset of fever did not reveal any
abnormal physical findings. Immunological screening on that day showed normal range of serum immunoglobulin levels (IgG: 833 mg/dL; IgA: 93 mg/dL; and IgM: 109 mg/dL), and serum complement levels (C3: 96 mg/dL; C4: 17 mg/dL; and CH50: 40.6 IU/L). CD2-positive T-cell/CD20-positive B-cell subset was normally distributed at 74%/17%.

Biochemical analysis of the isolate showed production of β-glucosidase, β-glucuronidase, and α-galactosidase. The isolate produced acid from trehalose and raffinose, but not from mannitol and glycogen. An API 20 Strep kit (Sysmex bioMérieux, Tokyo, Japan) identified the organism as *S. gallolyticus* subsp. *pasteurianus*. This was confirmed by 16S rRNA gene sequencing analysis, showing it to be 100% identical (1230 bp over the entire 1230 bp fragment) to that of the type strain ATCC43144. Furthermore, sequence type (ST) was determined using a method that has been recently established by us (13). Based on the allelic profiles of 7 housekeeping genes (*dpr, gmk, rpoD, parC, pta, pyrC*, and *recN*), this pathogen was categorized as a novel type of ST-58. This is one allele variant of ST-51 and belongs to a cluster of ST-14 complex (13). Fig. 1 illustrates UPGMA dendrogram genetic relationships among the isolates together with *S. gallootyticus* strains isolated elsewhere (13). MICs (μg/mL) of the various antimicrobial agents by the 2-fold serial dilution method in agar in accordance with Clinical and Laboratory Standards Institute guidelines (14) were as follows: penicillin G, ≤0.03; ampicillin, ≤0.06; ampicillin/sulbactam, ≤0.25; cefotaxime, ≤0.06; ceftiraxone, ≤0.06; cefepime, ≤0.5; chloramphenicol, ≤4; erythromycin, >1; clindamycin, >1; clarithromycin, >1; meropenem, ≤0.12; levofloxacin, 0.5; trimethoprim/sulfamethoxazole, ≤0.5; rifampicin, ≤1; linezolid, <2; and vancomycin, 0.5.

We presented a 3-year-old boy with bacteremia due to *S. gallootyticus* subsp. *pasteurianus*. This organism was subclassified and renamed as a subspecies of *S.*
*gallolyticus* based on biochemical characteristics in 2003 (1). Among the elderly or among patients with chronic disease, it can cause a variety of clinical syndromes, including bacteremia, endocarditis, meningitis, osteomyelitis, peritonitis, and solid organ abscess (2, 3). However, little is known about the clinical features of *S. gallolyticus* subsp. *pasteurianus* among children. We, therefore, reviewed the English literature through the Medline database using the terms *Streptococcus gallolyticus* subsp. *pasteurianus*, *Streptococcus bovis* biotype II/2, and children. We were able to find 23 of such pediatric cases (2-12). The clinical and microbiological features of these cases, as well as those of the present case, are summarized in Table 1. Most of them are sporadic cases, but a cluster of 5 preterm infants in a neonatal intensive care unit are included (7). Compared to those in adults (2, 3), childhood infections manifested as either meningitis or sepsis, and developed within 3 months of age, like as group B streptococcal infections (2, 4-12). In respect to age at onset, the present patient was the first case of eventual development of systemic infection far beyond 3 months of age.

This review also showed good prognosis in pediatric cases. All 19 patients with known outcomes survived without any sequelae (4-12). One meningitis case, which was complicated by grade 1 intracranial hemorrhage, was also free from sequelae at discharge (9). This may be, at least in part, attributable to good response to antimicrobial agents. All isolates from pediatric cases have been documented to be susceptible to penicillins, cefotaxime, and ceftriaxone (2-12), which have been widely used for the empirical treatment of infants with invasive bacterial infections.

In contrast to previous reports, one of the noteworthy features in the present case was spontaneous recovery without any treatment. Bacteremia is defined as the presence of viable microorganisms in the bloodstream and can be categorized as transient, intermittent, or persistent (15). *S. gallolyticus* is a commensal pathogen found in the intestinal tract in both humans and animals (1-3). The most plausible explanation of the
mechanism for systemic infection in our patient is breakdown of mucosal barriers as a result of rotavirus infection, which allowed entry of the organisms into the bloodstream. This pathogenesis is supported by previous patients with bacteremia, who presented with diarrhea as well as fever (7, 12). However, based on defervescence within 24 hours in our patient, bacteremia lasted for a few hours and was probably resolved by the natural immune system. Thus, the present case was categorized as transient bacteremia (15).

It should be noted that we obtained an appropriate amount of blood (3 ml) for culture after thorough skin antisepsis by 3% chlorhexidine gluconate. In addition, the Bactec Peds Plus/F culture bottle is a commercial pediatric bottle commonly used worldwide. The standard recommendation for culturing blood in this single bottle is based on its demonstrated superior recovery of pathogens and the infrequency of anaerobic pathogens in children (16). Furthermore, automated blood culture system showed a positive signal within 12 hours. Our blood culture results were thus indicative of genuine sepsis rather than an accidental contamination.

We recently thoroughly investigated a multilocus sequencing typing scheme for *S. gallolyticus* isolates collected from diverse origins and sources, and in different years (13). While STs of *S. gallolyticus* subsp. *gallolyticus* were significantly widely distributed, isolates of *S. gallolyticus* subsp. *pasteurianus* were classified into a single cluster, which almost entirely belonged to the ST-14 complex (13). The isolate from the present case was classified as a novel sequence type: i.e., ST-58. ST-58 is one allele variant of ST-51, also composed of the same ST-14 complex (Fig. 1). Taken together, strains of *S. gallolyticus* subsp. *pasteurianus* worldwide are suggested to have a relatively homogenous ST. However, further study is needed to determine which virulence factors (17) of *S. gallolyticus* subsp. *pasteurianus* are related to the ST-14 complex.
In conclusion, we described a case of transient bacteremia due to *S. gallolyticus* subsp. *pasteurianus* in a 3-year-old boy, who spontaneously recovered without antimicrobial treatment. The present case, for the first time, showed that this organism can cause invasive infection in a child aged far beyond 3 months. Our findings provide important information on epidemiology and public health of this rare infection.

**Conflict of interest** None to declare.
REFERENCES


**Figure legends**

Fig. 1. UPGMA dendrogram genetic relationships among ST14 complex, ST9 complex, and ST11 complex. *S. gallolyticus* subsp. *pasteurianus* isolates, including ours (ST58), belong to a single cluster, ST-14 complex. In contrast, ST9 complex and ST11 complex are two major ST complexes of *S. gallolyticus* subsp. *gallolyticus* isolates, including the type strain of *S. gallolyticus* ACM3611\(^\text{T}\). STs of these two *S. gallolyticus* subspecies are mutually exclusive. Allele profiles of each ST have been described by Shibata *et al.* (13).
<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Site(s) of isolation</th>
<th>Underlying condition</th>
<th>Antimicrobial agents, treatment duration</th>
<th>Outcome (complication)</th>
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