Resolution of *Pediococcus acidilactici* bacteremia without antibiotic therapy in a 16-year-old adolescent with leukemia receiving maintenance chemotherapy

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**A B S T R A C T**

*Pediococcus* spp. have been reported to cause infections in patients with underlying conditions. However, the pathogenicity of this bacteria is unclear. Herein, we describe the first case of *Pediococcus acidilactici* bacteremia, which occurred in a 16-year-old male with dasatinib-induced hemorrhagic colitis during maintenance therapy for leukemia and resolved without antibiotic treatment. *P. acidilactici* bacteremia might be self-limiting, even in immunocompromised patients receiving chemotherapy.

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**1. Introduction**

The *Pediococcus* spp. are catalase-negative, facultatively anaerobic, gram-positive cocci that are intrinsically resistant to vancomycin but mostly sensitive to beta-lactam antimicrobials. First discovered in foods such as beer, meat, and dairy products, these lactic acid bacteria are used as probiotics and are common members of the mammalian gut microbiota [1]. Their pathogenicity is believed to be low, but exceptions include invasive cases can cause sepsis, abscess formation, and infective endocarditis after abdominal surgery, during pregnancy, and in persons with hematological disorders [2–7]. The clinical significance of infections caused by this bacteria is unclear [4], although antibiotic therapy is indicated for infection in immunocompromised patients [2,7].

Herein, we report the first case of *Pediococcus* bacteremia, which occurred in a 16-year-old male who developed dasatinib-induced hemorrhagic colitis during maintenance therapy for leukemia. The disease resolved spontaneously without antibiotic therapy.

**2. Case Report**

A 16-year-old adolescent male on maintenance therapy for Philadelphia chromosome–positive acute lymphoblastic leukemia (Ph-ALL) presented to our hospital for evaluation of bloody stools, without abdominal pain, of several days’ duration. His medications included mercaptopurine, methotrexate, and dasatinib. He was also taking trimethoprim-sulfamethoxazole for *Pneumocystis* pneumonia prophylaxis. He had no past medical history of gastrointestinal disease and no history of abdominal surgery. He was eating yogurt almost daily. He had massive hematochezia and vomiting in the emergency department.

On examination, his vital signs were body temperature, 36.9 °C; blood pressure, 130/51 mm Hg; heart rate, 133/min; SpO2, 99% in room air; and respiratory rate, 18/min. The abdomen was soft and flat without tenderness. Laboratory testing showed a hemoglobin level of 6.3 g/dL, white blood cell count of 33 × 10⁹/L (65.5% neutrophils), and a platelet count of 113 × 10⁹/L. The prothrombin time/international normalized ratio was 1.02 and partial thromboplastin time was 24.2 s (control 28.0 s). Abdominal contrast-enhanced computed tomography showed a diffuse edematous colon wall and no obvious extravasation of contrast (Fig. 1). Total colonoscopy showed diffuse edematous mucosa and some reddening lesions, which suggested bleeding from the surface layer of the colon. There was no erosion, ulceration, or exposed vessels. Immunostaining of
biopsied mucosa was positive for cytomegalovirus. Although a cytomegalovirus antigenemia assay was weakly positive (1 positive cell/5 × 10^6 cells), dasatinib-induced hemorrhagic colitis was diagnosed based on gross colonoscopy findings. Maintenance therapy for Ph-ALL was discontinued and a blood transfusion was given. Upon admission, a set of blood cultures was obtained, namely, one aerobic pediatric bottle and one anaerobic bottle (BD BACTEC, Becton Dickinson and Company Sparks, MD, USA). After 24 h of incubation at 37 °C, gram-positive cocci were isolated in pairs from the aerobic bottle and in tetrads from the anaerobic bottle. Gram-positive cocci from the aerobic bottle were nonhemolytic and catalase-and oxidase-negative. Analysis with matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) using the VITEK MS system (bioMérieux SA, France) identified the pathogen as Pediococcus acidilactici. Antibiotic susceptibility was tested for vancomycin by agar disc diffusion, and no zone of inhibition was present. Gram-positive cocci from the anaerobic bottle were identified by partial 16S rRNA gene sequence analysis (Bacterial 16S rDNA PCR Kit Fast 800, Takara, Shiga, Japan) using the Basic Local Alignment Search Tool (BLAST). The isolate consensus sequence (527 bp) had the highest similarity (99.4% match) to Ruminococcus gnavus.

Because his general condition was improving when the positive blood culture results were received, we did not start antibiotic therapy. A subsequent blood culture was sterile. He had no hematocrit, fever, or abdominal pain after admission. He was discharged on hospital day 8, and maintenance therapy was resumed without dasatinib. One month later, he started imatinib instead of dasatinib. At a 4-month follow-up examination, he was well, with no evidence of recurrent Pediococcus infection.

3. Discussion

Our findings indicate that P. acidilactici bacteremia can resolve without antibiotics, even in an immunocompromised patient with leukemia receiving maintenance therapy. Pediococcus spp., although originally thought to be clinically insignificant [6], were first reported to be associated with human infection in 1987 [8]. Invasive cases have been reported in the settings of gastrointestinal tract injury, acute myeloblastic leukemia, metastatic adenocarcinoma of the gallbladder, and pregnancy [2,5,6,9]. All such cases were treated with antibiotics, but the clinical significance of infection is unclear because other bacteria were isolated from blood in most cases. Unlike the previous cases, our patient was asymptomatic, except for gastrointestinal bleeding, and a subsequent blood culture was sterile without the use of antibiotics. To our knowledge, there has been no report of spontaneous resolution of P. acidilactici bacteremia in patients with leukemia undergoing chemotherapy. Our case suggests that P. acidilactici bacteremia may not require antibiotic therapy, given the chance of self-resolution.

We hypothesize that pathogenesis began with disruption of the gastrointestinal mucosa by hemorrhagic colitis, resulting in transient bacteremia. The tyrosine kinase inhibitor dasatinib is a key drug in treating chronic myeloid leukemia and Philadelphia chromosome--positive acute lymphoblastic leukemia. However, gastrointestinal bleeding is a major side effect of this medication [10]. Bacterial translocation is defined as passage of bacteria from the gastrointestinal tract through the epithelial mucosa to mesenteric lymph nodes or other organs [11]. Probiotic use is associated with subsequent bacterial translocation and bacteremia. Lactobacillus rhamnosus GG, one of the most popular components of probiotic formulations, caused bacteremia after disrupting the intestinal mucosa in patients receiving corticosteroids and mesalazine for ulcerative colitis [12]. Because Pediococcus spp. can proliferate in the presence of pepsin or bile salts, bacterial translocation from the small and large intestines can occur. P. acidilactici also caused bacteremia in a 3-month-old infant who had consumed formula with added lactobacilli [13]. However, previously reported cases of P. acidilactici bacteremia were not associated with probiotic use. Additionally, there has been no report of bacteremia in consumers of dairy products.

The present pathological findings for the colon included cytomegalovirus positivity and a weakly positive result on an antigenemia assay. Treatment with antiviral drugs is usually needed for cytomegalovirus colitis in immunocompromised patients [14]. However, his hematochezia promptly improved without antiviral drugs after dasatinib was discontinued. Therefore, cytomegalovirus was likely not involved in the worsening of his condition. R. gnavus was also detected in his blood culture. It is a strict anaerobic gram-positive coccus commonly found in the gut microbiota [15]. A few cases of infection caused by this bacteria have been reported, but its pathogenicity is not fully understood [15]. In our patient, the bacteria spontaneously disappeared, which suggests low pathogenicity. R. gnavus is linked to inflammatory bowel disease [16]; however, our patient had no evidence of pathological inflammation suggesting inflammatory bowel disease.

In conclusion, to our knowledge, this is the first report of spontaneous resolution of P. acidilactici bacteremia in a Ph-ALL patient not treated with antibiotics. Although future cases will need to be studied before drawing firm conclusions, our findings suggest that P. acidilactici might be self-limiting, even in immunocompromised patients receiving chemotherapy.

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Ethical approval statement

This case report was consistent with the principles of the Declaration of Helsinki. Because this was an observational case report, the Ethics Committee of Niigata University confirmed that no ethical approval was required.

Authorship statement

All authors meet the ICMJE authorship criteria; JT, YA, RI and AS were responsible for the conception of the work. CS and CI were pediatric hematologists and in charge of the patient management and collected the data. JT and YA drafted the first manuscript. All
authors revised the work critically for important intellectual contents and approved the final version of this work.

Consent for publication

Written informed consent was obtained from the patient and his parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of Competing Interest

CI reports patent royalties from Juno Therapeutics, and the other authors have no conflicts of interest to disclose.

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