Lactobacillus Bacteremia Associated With Probiotic Use in a Pediatric Patient With Ulcerative Colitis

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Abstract: Probiotic strains of Lactobacillus are currently used in a variety of clinical practices with limited evidence to support their use. Lactobacillus species are a normal part of gastrointestinal flora, and bacteremia with probiotic strains of Lactobacillus is very uncommon. We describe a case of Lactobacillus bacteremia in a 17-year-old boy with ulcerative colitis managed with systemic corticosteroids and infliximab, who presented with fever to 102°F, flushing, and chills 1 week after starting Lactobacillus rhamnosus GG probiotics. Initial blood culture on day 2 of his fever was positive for Lactobacillus, however, subsequent blood cultures on day 3 and 5 were negative. He was treated empirically with antibiotics for 5 days and defervesced by day 8 of his illness. 16S rRNA sequence analysis identified the organism from the patient’s blood culture and probiotic capsule as L. rhamnosus with a 99.78% match for both the strains. This case report highlights the potential risk of Lactobacillus bacteremia in immunosuppressed patients with severe active ulcerative colitis.

Key Words: probiotics, Lactobacillus bacteremia, ulcerative colitis, inflammatory bowel disease

Lactobacillus is a gram-positive microaerophilic or facultative anaerobic rod-shaped bacterium that is a normal inhabitant of the human mouth, gastrointestinal flora, and genitourinary tract.1 Probiotic strains of Lactobacillus species are utilized in a variety of clinical practices with limited evidence to support their use. Eastern and Western medicine practitioners alike have proposed benefits of probiotics in treating diarrheal illnesses, irritable bowel syndrome, children with atopy, prevention of urogenital tract infections, and prevention of pouchitis in patients with inflammatory bowel disease.2–6 However, the mechanism of benefit of probiotics is not completely understood. It has been proposed that probiotics in the gastrointestinal tract may enhance intestinal barrier functions, stimulate immunity, and modulate inflammatory diseases.7–9 It has also been suggested that probiotics can inhibit infection and restore gut homeostasis by having a direct bactericidal effect on pathogenic bacteria and by inhibiting pathogen and toxin adhesion to the intestinal epithelium. Despite limited evidence, many patients use probiotics, believing in their efficacy without conferring with their physicians.

Serious infections with probiotic strains of Lactobacillus are very uncommon. The bacterial species are usually difficult to culture and identify and are typically considered contaminants.10 A few cases, however, have been reported mainly in immunocompromised hosts.11–13 To our knowledge, this is the first case of a probiotic strain isolated from the specimen was indistinguishable from the probiotic strain taken by the patient. We describe a case of Lactobacillus bacteremia in an immunosuppressed 17-year-old young man with severe ulcerative colitis (UC) who was taking Lactobacillus rhamnosus GG.

CASE PRESENTATION
A 17-year-old young man was diagnosed with UC after presenting with 6 weeks of hematochezia and 30 pound weight loss. Initially, his symptoms were attributed to traveler’s diarrhea and Clostridium difficile colitis. His symptoms persisted despite treatment with oral metronidazole and vancomycin and documented clearance of C. difficile. He was then diagnosed with UC after undergoing a colonoscopy showing pancolitis and MR enterography demonstrating abnormal thickening and enhancement of the colon with no evidence of small bowel involvement. He was refractory to intravenous methylprednisolone, but appeared to respond well to infliximab. After his initial hospitalization and diagnosis, he was managed as an outpatient with mesalamine and prednisone and appeared to be in stable condition. His parents provided him with a L. rhamnosus GG capsule (Culturelle—10 x 109 cells/capsule; ConAgra Foods, Omaha, NE) once daily.

Five days after receiving his first dose of infliximab, he developed high fevers to 102 to 104°F, flushing, and chills. His initial blood culture from an outside hospital was positive for Lactobacillus on day 2 of his fever, however, subsequent blood cultures on day 3 and 5 of his illness were negative before initiation of any antibiotic treatment. He continued to be febrile for 6 days and was admitted for intravenous antibiotics at that time. His sedimentation rate was 98 mm/h and C-reactive protein 9.1 mg/dL. He denied any diarrhea, emesis, abdominal pain, or respiratory symptoms. He was found to have a stool positive for C. difficile by polymerase chain reaction at the time of presentation for which he was treated with oral vancomycin. He was treated empirically with intravenous piperacillin/tazobactam and gentamicin for 5 days and defervesced by day 8 of his illness. A flexible sigmoidoscopy was performed with a report of nodularity and loss of vascular pattern in his left colon, sigmoid, and rectum. Biopsy results suggested mildly active chronic colitis with no granulomas identified. One week after his hospitalization, stool studies resulted positive for adenovirus antigen.

The bacterial isolates grown from the blood culture and the contents of the probiotic capsule of Culturelle the patient was taking were identified by conventional methods as Lactobacillus species. To obtain species-level identification of the Lactobacillus isolates, the organisms were analyzed with the ABI Prism 3130xl Genetic Analyzer (Life Technologies, Carlsbad, CA) using 16S rRNA sequence analysis.11 The isolates from the probiotic capsule and the blood culture were identified as L. rhamnosus with a 99.78% match for both strains. The phenotypic relatedness of the 2 L. rhamnosus isolates was determined by evaluating the profile of each strain’s susceptibility and resistance to a panel of antibiotics.12 Antimicrobial susceptibility testing was performed on both isolates...
by using the Clinical and Laboratory Standards Institute reference broth microdilution method\textsuperscript{13} on in-house-prepared panels. The results showed that the 2 strains of \textit{L. rhamnosus} shared nearly indistinguishable antibiograms. Of the 13 drugs tested on the panel, all were either the same or within 1 serial dilution, indicating a high probability that these 2 strains are identical (Table 1).

**TABLE 1.** Microbroth MICs for \textit{Lactobacillus rhamnosus} Strains Isolated From Probiotic Capsule and Blood Culture

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>\textit{Lactobacillus rhamnosus} (Probiotic Capsule) MIC (\mu g/mL)</th>
<th>\textit{Lactobacillus rhamnosus} (Blood Culture) MIC (\mu g/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>&gt;8</td>
<td>8</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&gt;8</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>&lt;0.12</td>
<td>&lt;0.12</td>
</tr>
<tr>
<td>Rifampin</td>
<td>&lt;0.25</td>
<td>&lt;0.25</td>
</tr>
<tr>
<td>Meropenem</td>
<td>&gt;2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>&lt;0.06</td>
<td>&lt;0.06</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Linezolid</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Trimeth/sulfa</td>
<td>&lt;0.25/5</td>
<td>&lt;0.25/5</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>&gt;4</td>
<td>&gt;4</td>
</tr>
</tbody>
</table>

MIC indicates minimum inhibitory concentration.

to consider the degree of disease activity and risk factors of the patient, such as concurrent enteric infections or recent use of immunosuppressive therapies, before administering probiotic therapy.

In general, there are no large clinical studies that have shown a strong benefit from probiotic therapy in pediatric patients with UC. Few studies including an open-label study and uncontrolled pilot study suggest induction and maintenance of remission in patients with UC who received VSL\textsuperscript{#3,20–22} however, they have small sample sizes and lack controls. A pediatric placebo controlled randomized study did demonstrate maintenance of remission in patients with active UC using VSL\textsuperscript{#3,23} however, the sample sizes were limited and further studies including larger randomized controlled trials are warranted.

This case should alert the reader to the possible danger of seemingly benign over-the-counter medications in UC and the need for proper communication between patients and their physicians. Although it has been proposed that probiotics can provide potential benefits in certain conditions, risks and benefits should still be carefully assessed before initiating this therapy in patients with UC, especially when they have severely active disease and may be immunocompromised.

**REFERENCES**