

## CASE REPORT

# A diagnostically challenging case of pyelonephritis caused by *Lactobacillus*

Erika Hori<sup>1</sup> | Michiyo Nakamura<sup>2</sup> | Hiroshi Tamura<sup>1</sup> 

<sup>1</sup>Department of Pediatrics, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan

<sup>2</sup>Kumamoto University Hospital Nursing Department, Kumamoto, Japan

**Correspondence**

Hiroshi Tamura, Department of Pediatrics, Faculty of Life Sciences, Kumamoto University, 1-1-1 Honjo, Kumamoto 860-8556, Japan.  
Email: [bohm1905ht@kuh.kumamoto-u.ac.jp](mailto:bohm1905ht@kuh.kumamoto-u.ac.jp)

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**Abstract**

Extracellular polysaccharides produced by *Lactobacillus* have been shown to stimulate the immune system, suppress reactivity to allergens, and protect from infections; these properties underlie the use of *Lactobacillus* in probiotic formulations and in the prevention and treatment of urinary tract infections. However, *Lactobacillus* can be independently isolated at high numbers from sites of infection and has been rarely considered as the causative agent of infections in immunocompromised individuals. We herein report the case of a 46-year-old female patient who developed pyelonephritis due to *Lactobacillus* following total thyroidectomy for papillary thyroid cancer. The patient also had to fast due to post-operative vocal cord paralysis and received steroid treatment. As illustrated in the clinical course of our patient, *Lactobacillus* can be overlooked as a contaminant in culture samples and should be suspected as the etiology of infection especially in patients with weakened immune responses. We suggest that the detection of *Lactobacillus* in culture these patients might be an indication to initiate appropriate antibiotic treatment without delay.

**KEYWORDS**

immunocompromised host, *Lactobacillus*, pyelonephritis

## 1 | INTRODUCTION

Bacteria belonging to the *Lactobacillus* genus are well known for their role in fermenting milk to produce yogurt and are thus known as yogurt lactic acid bacteria.

These bacteria are commonly found in intestinal flora, vagina, and oral cavity and are considered as contaminants in cultures.<sup>1,2</sup> Intravaginal administration of *Lactobacillus* is used to prevent recurrent urinary tract infections.<sup>3,4</sup> Indeed, in the genitourinary system, vaginal colonization by *Lactobacillus* provides a natural and non-specific defense mechanism against various infections. Lactate production results in a local decrease in pH, which

in combination with the hydrogen produced by symbiotic anaerobic bacteria prevents vaginal mucosal colonization by apathogenic bacteria. Further, *Lactobacillus* interferes with the attachment of potential pathogens by producing biosurfactants, such as succinate and other anti-adhesion surface-active proteins.<sup>4-6</sup> Because of these properties, *Lactobacillus* is used in probiotic formulation, and it is believed that the use of *Lactobacillus* represents an effective approach for the prevention as well as treatment of urinary tract infections.<sup>4,7</sup>

Due to its low pathogenicity, *Lactobacillus* has been very rarely reported as a causative agent of infectious diseases in humans with normal immunity.<sup>3</sup> However, several

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studies reported endocarditis, meningitis, and postoperative infections, among others, caused by *Lactobacillus* in patients with weakened immune function.<sup>8–10</sup> Herein, we report the case of a 46-year-old female patient who developed pyelonephritis due to *Lactobacillus* following total thyroidectomy for papillary thyroid cancer.

## 2 | CASE REPORT

Here we report the case of a 46-year-old Japanese female patient with an increase in the left cervical lymph node who visited a nearby otolaryngologist. For further scrutiny, she was referred to our otolaryngology department 3 months before her surgery. At the time of consultation, echography revealed the swelling of the left cervical lymph nodes and the calcification of the thyroid gland. A diagnosis of papillary thyroid cancer (cT1N1bM0) was made using pathological examination. She underwent total thyroidectomy and left-sided lymph node dissection for papillary thyroid cancer. The left recurrent laryngeal nerve, which was dissected during the operation, was immediately repaired by suture; however, the patient developed bilateral recurrent laryngeal nerve palsy and required tracheostomy during the operation in the Department of Otolaryngology. Her one parathyroid gland was preserved during the operation. For recurrent laryngeal nerve palsy, hydrocortisone sodium succinate (300 mg/day, 200 mg/day, 100 mg/day) infusion was administered for 3 days after the operation and oral prednisolone (30 mg/day) was initiated on postoperative day four. Prednisolone dose was gradually tapered (20 mg/day; 2 days, 10 mg/day; 3 days,

5 mg/day; 3 days) and discontinued at the time of discharge 12 days after the operation.

The day after discharge, the patient developed a fever of 38.2°C, severe pain in right shoulder blade, stomach discomfort, and malaise. Bacterial infection was suspected based on an elevated white blood cell (WBC) count of 11,100/L and an increased C-reactive protein (CRP) level of 3.11 mg/dl. No abnormalities were noted in the neck area with ultrasound echo examination. Chest computed tomography and gastroscopy did not reveal any abnormalities. Sputum sample was collected for culture, and garenoxacin (400 mg/day) was started as oral antibiotic treatment.

Two days later, the patient was referred to our department for further investigation due to persistent fever, elevated WBC count (14,900/L), and slightly elevated CRP level (5.90 mg/dl). Her vitals at the time of referral were as follows: weight, 57.9 kg; height, 163.5 cm; body mass index, 21.7 kg/m<sup>2</sup>; body temperature, 39.4°C; blood pressure, 111/91 mm Hg; pulse, 90 beats/min; respiratory rate, 24 breaths/min; oxygen saturation, 99% in room air. Tenderness was noted in right-side costovertebral angle and suprapubic area. Laboratory tests revealed a blood urea nitrogen level of 13 mg/dl (normal range, 8–20 mg/dl) and a serum creatinine level of 0.91 mg/dl (normal range, 0.46–0.79 mg/dl). Urinalysis revealed 1–4 red blood cells/high-power field and 1–4 white blood cells/high-power field. Due to the slight increase in serum creatinine in the absence of abnormalities in the urine sediment, urinary tract infection was suspected and a sample was collected for urine culture analysis. The previously initiated garenoxacin was considered to be ineffective, and treatment was discontinued after a total treatment duration of 3 days.

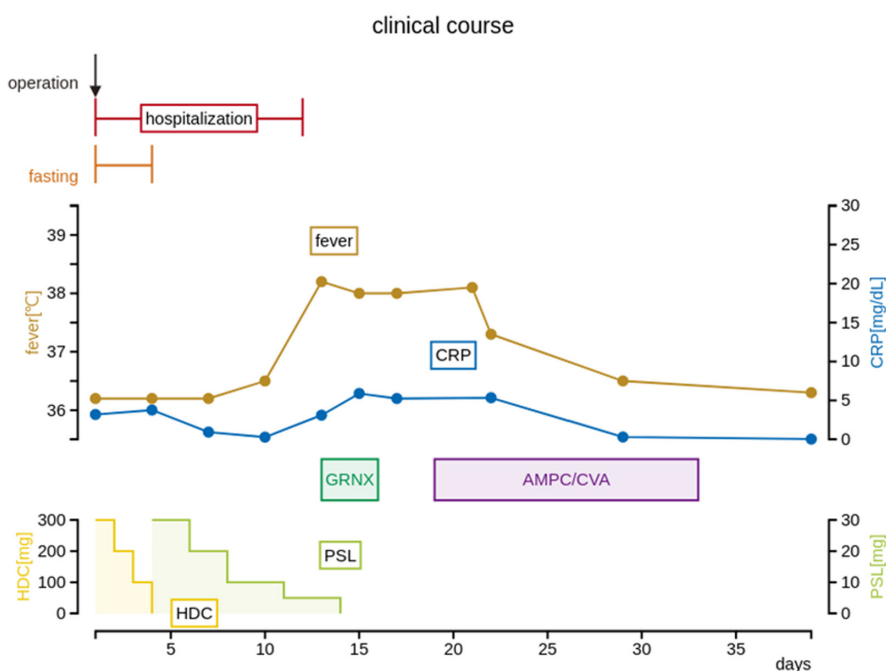


FIGURE 1 Fever, C-reactive protein (CRP), and the treatment during the observation period

Two days after the referral, the fever and right shoulder pain had not change although there was a slight decrease in WBC count (9200/L) and CRP level (5.22 mg/dl). Another sample was collected for urine culture, but no antibiotics were administered. The first urine culture collected at the time of referral was positive for *Lactobacillus*, and contamination was considered. The second urine culture was positive for Gram-positive rods. Therefore, the patient was diagnosed with urinary tract infection and oral antibiotic treatment was initiated with amoxicillin hydrate/potassium clavulanate (1000 mg/day) 4 days after referral, based on the sensitivity of *Lactobacillus*. Three days after the second urine culture was submitted, *Lactobacillus* was found to be positive. The fever disappeared after 5 days of oral antibiotic treatment, and the patient completed a 14-day course of antibiotic treatment. The clinical course of the patient is summarized in Figure 1.

### 3 | DISCUSSION

In a study analyzing 543,765 blood culture-positive samples, Franko et al. reported that *Lactobacillus* was detected in 121 samples, accounting for 0.34% of all cases.<sup>11</sup> Malignant tumors and immune compromise were the most common underlying diseases in 38 patients with *Lactobacillus*-positive samples.<sup>11</sup> In a report by Lee et al., *Lactobacillus salivarius* was the most frequently detected bacterium in 89 patients with *Lactobacillus* bacteremia; however, only approximately 50% of the patients received appropriate antibiotic treatment.<sup>12</sup> Furthermore, the subsequent mortality rate was high, between 21% and 62%, even following negative results in blood cultures with appropriate treatment.<sup>13</sup> One proposed reason for this outcome is the presence of an underlying disease in patients infected with *Lactobacillus* who often harbor coinfection with other bacteria. The detection of *Lactobacillus* in blood cultures might be an indication to initiate appropriate antibiotic treatment without delay.<sup>13</sup> In the present case, garenoxacin was started before the first urinalysis; therefore, no increase in leukocytes was observed in the subsequent analysis of urine sediment. The patient exhibited only fever and malaise and did not complain of back pain; however, pyelonephritis was suspected based on a slight increase in creatinine and the urine culture results suggested *Lactobacillus* contamination. However, *Lactobacillus* was also detected in the second urine culture. *Lactobacillus* infection was suspected, and the antibiotic was changed to amoxicillin hydrate / potassium clavulanate. The sensitivity of the patient to the selected antibiotics was confirmed, and the clinical condition

of the patient exhibited steady improvement following treatment.

Our review of the literature identified a total of 11 case reports of patients with pyelonephritis due to *Lactobacillus*, including the current case (Table 1). The age ranged from 41 to 94 years (median, 59 years), and there were 9 female and 2 male patients. Among the 11 cases, 6, 4, 4, and 3 patients had a history of diabetes, cancer, hypothyroidism, and urolithiasis, respectively. In previous reports, *Lactobacillus* infection from a renal source was associated with predisposing underlying conditions such as diabetes, neutropenia, cancer, and urolithiasis, whereas risk factors included certain antibiotics and immunocompromizing conditions, such as the use of certain steroids.<sup>14–18</sup> These findings were similar to those observed in the current case.

The etiology of *Lactobacillus* infection from renal sources is likely multifactorial. First, in immunocompetent individuals, *Lactobacillus* infection is considered to induce local and systemic immune responses and enhance mucosal function.<sup>19</sup> However, impaired mucosal function in certain clinical settings can increase the susceptibility of at-risk individuals to *Lactobacillus* infection. For example, urinary stones cause urinary congestion and increase the risk of urinary tract infections<sup>20</sup> whereas uncontrolled diabetes can cause angiopathy, renal papillary necrosis, and nephropathy, which can also increase the risk of *Lactobacillus* infection.<sup>21</sup>

Second, the use of certain antibiotics can select for *Lactobacillus* species and cause infection in sensitive individuals. Studies show that *Lactobacillus* exhibits almost uniform resistance to trimethoprim-sulfamethoxazole and ciprofloxacin, with general resistance to vancomycin, metronidazole, and third-generation cephalosporins.<sup>22,23</sup> Third, Prednisolone suppresses a variety of immune responses including cell-mediated and humoral immunity and decreased cytokine production. The prevalence increases in a dose-dependent manner, and opportunistic infections increase rapidly at higher prednisolone doses.<sup>24</sup>

Surprisingly, our literature review revealed that the four patients with available detailed medical history had hypothyroidism. Preclinical studies reveal that thyroid hormone itself acts on and activates immune cells and plays a major role in protection from infections. Therefore, the defense against infection is weakened in patients with hypothyroidism.<sup>25,26</sup>

In the present case, the young patient who was previously healthy was considered to develop an opportunistic *Lactobacillus* infection due to several underlying causes, including immunosuppression caused by hypothyroidism following total thyroidectomy performed for papillary thyroid cancer, fasting due to postoperative vocal cord paralysis, and steroid treatment.

TABLE 1 Characteristics of the 11 reported cases of *Lactobacillus* urinary tract infections

Age	Sex	Clinical features	Predisposing condition	Treatment <sup>a</sup>	Reference
41	F	Fever Right lower back pain	Type 2 diabetes	Ceftriaxone → Subactam/ampicillin	3
46	F	Fever Right shoulder pain	Postoperative Thyroid papillary cancer Hypothyroidism Steroid	Levofloxacin → Amoxicillin clavulanic acid	This case
51	F	Fever Left flank pain	Type 2 diabetes Hypertension Brest carcinoma	Vancomycin → Clindamycin	14
52	F	Fever Right flank pain	Right nephrectomy for urolithiasis	Gentamicin Ampicillin → Ampicillin	13
59	F	Fever Left lumbar pain	Lymphoma Type 2 diabetes Hypertension	Gentamicin → Ampicillin	10
63	F	Fever Right flank pain	Urolithiasis with hydronephrosis Urothelial carcinoma	Levofloxacin Ciprofloxacin → Clindamycin	15
68	F	Fever Nausea Left-sided flank pain pyelonephritis	Type 2 diabetes Left urolithiasis Hypothyroidism	Ciprofloxacin → Amoxicillin	9
85	F	Painful voiding frequency urgency cystitis	Postoperative cystocele Hypothyroidism	Ciprofloxacin → Clarithromycin	22
94	F	Urinary incontinence diffuse abdominal pain cystitis	Type 2 diabetes Hypothyroidism	Fosfomycin Ciprofloxacin → Amoxicillin clavulanic acid	23
49	M	Dysuria Pelvic pain	Acute prostatitis	Cefotaxime → Amoxicillin	26
66	M	Fever	Diabetes Arteriosclerosis	Cefotaxime → Amoxicillin	11

<sup>a</sup>First Antimicrobial (resistance)→Final Antimicrobial (susceptibility).

## 4 | CONCLUSION

Albeit a rare pathogen, *Lactobacillus* can lead to serious infection in individuals with multiple predisposing factors. Therefore, individuals with risk factors, such as steroid use, and those with immunocompromised conditions, such as hypothyroidism and cancer, should be promptly evaluated, and appropriate treatment should be initiated without delay if the culture test is positive for *Lactobacillus*.

### AUTHOR CONTRIBUTIONS

EH and HT: treated the patient. MN and HT performed the analysis. EH wrote the paper.

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### CONFLICT OF INTEREST

None declared.

### DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

### ETHICAL APPROVAL

All the procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards (64th WMA General Assembly, Fortaleza, Brazil, October 2013). Informed consent for examinations and to publish their cases, including images was obtained from patients and/or their family members.

### CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

### ORCID

Hiroshi Tamura  <https://orcid.org/0000-0001-8786-217X>

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