Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.9611-17
Intern Med 57: 1469-1473, 2018
http://internmed.jp

【 CASE REPORT 】

Raoultella planticola Bacteremia in a Patient with Early Gastric Cancer

Shotaro Yamamoto[1,2], Katsuya Nagatani[1], Takeo Sato[1], Takeyoshi Ajima[2] and Seiji Minota[1]

Abstract:
The patient was an 81-year-old man who was found to have bacteremia due to *Raoultella planticola*, which might have entered the circulation through the bile duct during the passing of a gallbladder stone. In the present case, we screened for malignancies because most cases of *R. planticola* bacteremia occur after trauma, invasive procedures, or in patients with malignancy (70.6%). Early gastric cancer was detected. Although the association between *R. planticola* bacteremia and malignancy remains speculative in the present case, it may be useful to scrutinize similar cases involving low-virulence bacteremia for possible malignancies or immune conditions.

Key words: bacteremia, gastric cancer, malignancy, *Raoultella planticola*

(Intern Med 57: 1469-1473, 2018)
(DOI: 10.2169/internalmedicine.9611-17)

Introduction

Raoultella planticola is a gram-negative rod, aerobic, non-motile, and capsulated bacterium that was first described as *Klebsiella planticola* in 1981 (1, 2). *R. planticola* is included in the Enterobacteriaceae family and has a histidine decarboxylase enzyme that produces histamine from histidine; thus, it can cause histamine fish poisoning (3). In 2001, it was reclassified as *R. planticola* based on a 16S rRNA and *rpoB* gene analysis (2). *R. planticola* was initially identified as an environmental bacterium of aquatic, botanic, and soil systems (1, 4). *R. planticola* is generally harmless and rarely causes infection in humans. It colonizes 9-18% of humans, mainly in the urine, feces, and sputum (5, 6). Two cases of infection by *R. planticola* were first reported in 1984 (7). Since then, cases of *R. planticola* infection have been reported in humans with trauma, malignancy, and gastroenteritis after consuming poorly prepared fish and after invasive medical examinations (5, 8-10). Although both immunocompetent and immunocompromised hosts can develop *R. planticola* bacteremia, 82.4% of patients are immunocompromised.

We herein report a case of *R. planticola* bacteremia that seemed to be a complication of gallbladder stones and bile duct damage. Because of the rarity of *R. planticola* bacteremia in immunocompetent patients, we screened for possible malignancies and detected early gastric cancer.

Case Report

The patient was an 81-year-old Japanese who presented to our hospital with chills, anorexia, and fatigue that had persisted for several days. He also described intermittent and piercing abdominal pain. He had a history of coronary spastic angina, for which he had been taking diltiazem.

A physical examination at the first visit revealed the following findings: blood pressure, 139/61 mmHg; pulse rate, 55 beats per minute; body temperature, 38.1℃; respiration rate, 24 per minute; and percutaneous oxygen saturation, 95% under room air. The patient's consciousness was clear. The abdominal pain had already subsided and he did not have any abdominal tenderness and his system review was unremarkable. Routine laboratory tests were performed because of his advanced age, and due to the presence of fever, and tachypnea. Routine laboratory tests revealed a decreased platelet count (9.1×10^4/μL) and elevated levels of C-reactive protein (26.3 mg/dL), aspartate transaminase (233 U/L),

[1]Division of Rheumatology and Clinical Immunology, Department of Medicine, Jichi Medical University, Japan and [2]Division of Internal Medicine, Jinsekikogen Town Hospital, Japan
Received: June 4, 2017; Accepted: August 29, 2017; Advance Publication by J-STAGE: December 27, 2017
Correspondence to Dr. Shotaro Yamamoto, m06100sy@jichi.ac.jp

Table 1. Laboratory Data on Admission.

Leukocytes (×10³/μL)	7.0 (3.7 - 7.0)	AST (U/L)	233 (13 - 33)
Neutrophils (%)	85.9 (41.6 - 68.2)	ALT (U/L)	155 (8 - 42)
Eosinophils (%)	0 (0.1 - 4.2)	LDH (U/L)	477 (119 - 229)
Basophils (%)	0.4 (0 - 1.0)	γ-GT (U/L)	127 (11 - 58)
Monocytes (%)	8.4 (4.9 - 9.7)	ALP (U/L)	303 (115 - 359)
Lymphocytes (%)	5.2 (23.1 - 44.7)	T. Bil (mg/dL)	1.0 (0.2 - 1.2)
Hemoglobin (g/dL)	14.6 (14.1 - 17.0)	BUN (mg/dL)	34 (8 - 22)
Platelets (×10⁴/μL)	9.1 (15.9 - 30.0)	Cr (mg/dL)	1.2 (0.6 - 1.1)
CRP (mg/dL)	26.3 (<0.2)	FDP (μg/dL)	13.7 (<5.0)
CK (U/L)	3,278 (62 - 287)	PT-INR	1.05

CRP: C-reactive protein, CK: creatine phosphokinase, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, γ-GT: γ-glutamyltranspeptidase, ALP: alkaline phosphatase, T. Bil: total bilirubin, BUN: blood urea nitrogen, Cr: creatinine, FDP: fibrin degradation products, PT-INR: prothrombin time-international normalized ratio

Table 2. Susceptibility of *R. planticola* in the Present Case.

Agent	Susceptibility	MIC (μg/mL)
Amoxicillin	R	>16
Ampicillin	R	>16
Amoxicillin/clavulanate	S	≤8
Ampicillin/sulbactam	S	≤8
Piperacillin/tazobactam	S	≤16
Cefazolin	S	≤2
Ceftazidime	S	≤4
Cefmetazole	S	≤16
Ceftriaxone	S	≤1
Cefepime	S	≤2
Imipenem	S	≤0.5
Meropenem	S	≤0.5
Gentamicin	S	≤4
Minocycline	S	≤4
Ciprofloxacin	S	≤0.06
Levofloxacin	S	≤0.12
Trimethoprim/sulfamethoxazole	S	≤40

R: resistant, S: susceptible, MIC: minimum inhibitory concentration

alanine transaminase (155 U/L), lactate dehydrogenase (477 U/L), γ-glutamyltranspeptidase (127 U/L), creatinine kinase (3,278 U/L), and fibrin degradation product (13.7 μg/dL) (Table 1). Abdominal ultrasonography and plain CT of the chest, abdomen, and pelvis showed two stones of 5 mm and 8 mm in diameter in the gallbladder. The patient was admitted to our hospital based on the suspicion of a bacterial infection of unknown nature and rhabdomyolysis. Antibiotic therapy was started empirically with intravenous ampicillin-sulbactam (4.5 g daily) after drawing two sets of blood specimens for bacterial culturing. On the third hospital day, two sets of blood cultures were found to be positive for *R. planticola*. The bacterium was susceptible to ampicillin-sulbactam, cefazolin, ceftriaxone, and levofloxacin, but not ampicillin or amoxicillin (Table 2). Although the entry focus of *R. planticola* was unknown, his constitutional symptoms and laboratory data, including his liver function, improved after a total of 14 days of antibiotic therapy (initially with ampicillin-sulbactam, then with ceftriaxone). He also recovered from rhabdomyolysis without aftereffects with fluid replacement alone, and his creatine phosphokinase (CK) level returned to 258 U/L (within the normal range) on the 4th hospital day. He was discharged on the 15th hospital day.

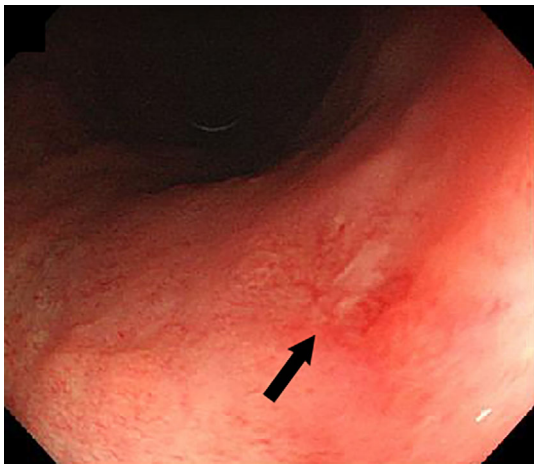

Figure. Upper gastrointestinal endoscopy showed an ulcerative lesion in the upper gastric body of the lesser curvature (arrow).

Upper gastrointestinal endoscopy was performed for screening purposes, because most patients with *R. planticola* bacteremia are either immunocompromised or cancer-bearing. An ulcerative lesion was found at the lesser curvature of the upper gastric body (Figure), and a histological examination showed well-differentiated tubular adenocarcinoma. A biopsy of the ulcer showed no sign of *Helicobacter pylori* infection, and the specimen was negative for IgG antibody to *H. pylori*. He was referred to another hospital that specialized in gastroenterology for further examinations and treatment.

Discussion

R. planticola is a type of commensal bacteria. It is rarely associated with serious infections in humans. In recent years, however, the number of *R. planticola* infections has been increasing. The incidence of *R. planticola* infection

Table 3. **Reported Cases of *R. planticola* Bacteremia.**

Reference	Age / Sex	Comorbidity	Invasive procedures	Antibiotics	Outcome
7	69 / F	Mitral stenosis	Mitral valve replacement	Tobramycin and cefotaxime	Recovered
6	57 / N/A	N/A	Post-CABG	Ceftriaxone	Recovered
11	83 / F	N/A	N/A	Moxifloxacin, ceftriaxone, azithromycin, and meropenem	Died
11	64 / M*	B cell lymphoblastic lymphoma	N/A	Doxycycline	Died
16	65 / M	Advanced apocrine adenocarcinoma	ERCP	Cefoperazone / sulbactam, meropenem, and piperacillin / tazobactam	Recovered
17	59 / M	Pancreatic carcinoma	ERCP	Piperacillin / tazobactam	Recovered
24	75 / M	Pancreatic carcinoma	N/A	Cefotaxime and metronidazole	Died
10	63 / M	Hypercholesterolemia, BPH, and Posterior pituitary adenoma	N/A	Piperacillin / tazobactam and Cefotaxime	Recovered
12	70 / M*	Pancreatic adenocarcinoma, COPD, and Bronchiectasis	N/A	Ciprofloxacin and metronidazole	Recovered
13	57 / M*	Non-small-cell lung cancer with multiorgan metastasis	N/A	Levofloxacin, gentamicin, and ceftazidime	Recovered
14	56 / F*	Non-small-cell lung cancer with liver metastases	N/A	Ceftriaxone and metronidazole	Recovered
15	51 / F*	Multiple myeloma	N/A	Ciprofloxacin	Recovered
15	69 / F*	Cervical cancer	N/A	Ceftriaxone and ciprofloxacin	Recovered
15	64 / M*	Cholangiocarcinoma	N/A	Piperacillin / tazobactam	Recovered
15	64 / M*	Acute myeloid leukemia	Central line	Cefepime	Recovered
15	59 / M	AMI, ROSC after cardiac arrest	Central line	Vancomycin and imipenem	Died
15	66 / F*	Gallbladder adenocarcinoma	N/A	Piperacillin / tazobactam	Recovered
15	81 / M*	Cholangiocarcinoma	N/A	Piperacillin / tazobactam and levofloxacin	Recovered
15	72 / M	Hepatocellular carcinoma	N/A	No treatment	Died
15	59 / M*	Multiple myeloma	N/A	Cefepime and metronidazole	Recovered
15	54 / F*	Cervical cancer	N/A	Meropenem and tobramycin	Died
15	69 / F	Diabetes mellitus	N/A	Ciprofloxacin	Recovered
15	60 / F*	Diffuse large B cell lymphoma	N/A	Vancomycin and cefepime	Recovered
15	75 / F*	Gallbladder adenocarcinoma	N/A	Ceftriaxone and metronidazole	Recovered
15	78 / F*	Cholangiocarcinoma	N/A	Ceftriaxone and metronidazole	Recovered
15	53 / F*	Gallbladder adenocarcinoma	N/A	Ceftriaxone and metronidazole	Recovered
15	65 / M*	Pancreatic adenocarcinoma	N/A	Ceftriaxone and metronidazole	Recovered
15	69 / F	Nonspecific	N/A	Ceftriaxone and metronidazole	Recovered
15	18 / M*	B cell lymphoblastic lymphoma	Central line	Cefepime and teicoplanin	Recovered
15	75 / M*	Cholangiocarcinoma	N/A	Piperacillin / tazobactam	Recovered
15	21 / M*	Acute myeloid leukemia	Central line	Meropenem and cefepime	Recovered
25	11 month / N/A	N/A	N/A	N/A	N/A
9	52 / M	Chronic pancreatitis, HT, and CRD	N/A	N/A	Died
26	62 / M	DM, HT, and BPH	N/A	Piperacillin / tazobactam, ceftriaxone, and ciprofloxacin	Recovered
Our case	81 / M	Coronary spastic angina and gastric carcinoma	None	Ampicillin / sulbactam and ceftriaxone	Recovered

* The patient was treated with chemotherapy or stem cell transplantation.

M: male, F: female, N/A: not available, CABG: coronary artery bypass grafting, ERCP: endoscopic retrograde cholangiopancreatography, BPH: benign prostatic hypertrophy, COPD: chronic obstructive pulmonary disease, AMI: acute myocardial infarction, ROSC: return of spontaneous circulation, HT: hypertension, CRD: chronic renal disease, DM: diabetes mellitus

might have previously been underestimated due to the difficulty in isolating the bacterium and confusion with other bacteria, including *Klebsiella* spp. (7).

In the present case, *R. planticola* was detected in the blood, but the focus of bacterial entry was unknown. The abdominal pain, elevated liver enzyme levels, and the presence of gallbladder stones indicated the passage of gallbladder stones through the bile duct, and retrograde infection during this process was a possibility; the gastrointestinal tract is the site of *R. planticola* colonization and no other focus of infection was found in the present case.

We only found 34 cases of *R. planticola* bacteremia in our review of the literature (Table 3). The median patient age was 64 years (range: 11 months to 83 years) and the ra-

tio of males was 59.4%. Seven of 34 patients (20.6%) died of *R. planticola* bacteremia. Twenty-four of 34 (70.6%) patients also had a malignancy. The malignancies included hematological malignancies (n=7, 29.2%), biliary tract neoplasms (n=7, 29.2%), pancreatic neoplasms (n=4, 16.7%), and others (n=6, 25.0%). Twenty of 24 patients (83.3%) with malignancies were treated with chemotherapy or stem cell transplantation (11-15) before the development of bacteremia. Thus, an immunocompromised state - due to either a malignancy itself or the associated chemotherapy - appears to be associated with the development of *R. planticola* bacteremia. Eight of 34 (23.5%) patients received invasive medical procedures such as endoscopic retrograde cholangiopancreatography, central venous catheterization, and cardiovascular surgical procedures (6, 7, 15-17). It is noteworthy that 14 of 34 (41.2%) patients had a malignancy or a history of invasive medical procedures to the hepatobiliary system or pancreas, indicating that the hepatobiliary system or pancreas is one of the foci of *R. planticola* bacteremia.

R. planticola is usually susceptible to most antibiotics except ampicillin. However, recently, *R. planticola* with resistance to carbapenems or with extended spectrum β lactamase has been reported (18, 19). In two of the cases in Table 3, *R. planticola* was resistant to carbapenems (11, 13). In one of these two cases, *R. planticola* was susceptible to gentamicin, levofloxacin, and tetracycline (11); in the other, it was susceptible to fluoroquinolone, aminoglycoside, and colistin (13). Based on these findings, aminoglycoside or fluoroquinolone may appropriate choices of antibiotics for carbapenem-resistant *R. planticola*.

Some bacteria are considered to be related to malignancy. For example, *Streptococcus gallolyticus* subsp. gallolyticus (SGG), which was formerly named *Streptococcus bovis* biotype I, and *Clostridium septicum* bacteremia are associated with colorectal malignancy (20). In addition to colonizing colorectal neoplasms and invading the blood from the damaged mucosa, SGG may also actually cause colorectal malignancies. On the other hand, *C. septicum* bacteremia occurs through mucosal damage caused by carcinoma (21-23). Although the cause-and-effect relationship between *R. planticola* bacteremia and malignancy is unknown, the literature suggests that *R. planticola* bacteremia occurs in patients who are immunocompromised as a result of malignancy. We need to accumulate additional cases of *R. planticola* bacteremia to clarify the relationship between *R. planticola* and early-stage cancer.

It is intriguing to consider the cause-and-effect relationship between *R. planticola* bacteremia and early gastric cancer in the present case. Although the association remains elusive, the fact that most patients with *R. planticola* bacteremia are immunocompromised or cancer-bearing led us to screen for malignancies; the patient happened to have gastric cancer without any symptoms. Thus, when we encounter such patients, it may be worthwhile to screen for malignancies.

The authors state that they have no Conflict of Interest (COI).

References

1. Susan TB, Ramon JS, Don JB. *Klebsiella planticola* sp. nov.: A new species of enterobacteriaceae found primarily in nonclinical environments. Curr Microbiol **6**: 105-109, 1981.
2. Drancourt M, Bollet C, Carta A, Rousselier P. Phylogenetic analyses of *Klebsiella* species delineate *Klebsiella* and *Raoultella* gen. nov., with description of *Raoultella ornithinolytica* comb. nov., *Raoultella terrigena* comb. nov. and *Raoultella planticola* comb. nov. Int J Syst Evol Microbiol **51**: 925-932, 2001.
3. Kanki M, Yoda T, Tsukamoto T, Shibata T. *Klebsiella pneumoniae* produces no histamine: *Raoultella planticola* and *Raoultella ornithinolytica* strains are histamine producers. Appl Environ Microbiol **68**: 3462-3466, 2002.
4. Ferragut C, Izard D, Gavini F, Kersters K, Deley J, Leclerc H. *Klebsiella trevisanii*: a new species from water and soil. Int J Syst Bacteriol **33**: 133-142, 1983.
5. Ershadi A, Weiss E, Verduzco E, Chia D, Sadigh M. Emerging pathogen: a case and review of *Raoultella planticola*. Infection **42**: 1043-1046, 2014.
6. Freney J, Gavini F, Alexandre H, et al. Nosocomial infection and colonization by *Klebsiella trevisanii*. J Clin Microbiol **23**: 948-950, 1986.
7. Freney J, Fleurette J, Gruer LD, Desmonceaux M, Gavini F, Leclerc H. *Klebsiella trevisanii* colonisation and septicaemia. Lancet **1**: 909, 1984.
8. Kim SW, Kim JE, Hong YA, Ko GJ, Pyo HJ, Kwon YJ. *Raoultella planticola* peritonitis in a patient on continuous ambulatory peritoneal dialysis. Infection **43**: 771-775, 2015.
9. de Campos FP, Guimarães TB, Lovisolo SM. Fatal pancreatic pseudocyst co-infected by *Raoultella planticola*: an emerging pathogen. Autops Case Rep **6**: 27-31, 2016.
10. Puerta-Fernandez S, Miralles-Linares F, Sanchez-Simonet MV, Bernal-Lopez MR, Gomez-Huelgas R. *Raoultella planticola* bacteraemia secondary to gastroenteritis. Clin Microbiol Infect **19**: E236-E237, 2013.
11. Castanheira M, Deshpande LM, DiPersio JR, Kang J, Weinstein MP, Jones RN. First descriptions of bla_{KPC} in *Raoultella* spp. (*R. planticola* and *R. ornithinolytica*): report from the SENTRY Antimicrobial Surveillance Program. J Clin Microbiol **47**: 4129-4130, 2009.
12. Salmaggi C, Ancona F, Olivetti J, Pagliula G, Ramirez GA. *Raoultella planticola*-associated cholangitis and sepsis: a case report and literature review. Q J Med **107**: 911-913, 2014.
13. Tseng SP, Wang JT, Liang CY, Lee PS, Chen YC, Lu PL. First report of bla_{IMP-8} in *Raoultella planticola*. Antimicrob Agents Chemother **58**: 593-595, 2014.
14. Lam PW, Salit IE. *Raoultella planticola* bacteremia following consumption of seafood. Can J Infect Dis Med Microbiol **25**: e83-e84, 2014.
15. Chun S, Yun JW, Huh HJ, Lee NY. Low virulence? Clinical characteristics of *Raoultella planticola* bacteremia. Infection **42**: 899-904, 2014.
16. Yokota K, Gomi H, Miura Y, Sugano K, Morisawa Y. Cholangitis with septic shock caused by *Raoultella planticola*. J Med Microbiol **61**: 446-449, 2012.
17. Hu AY, Leslie KA, Baskette J, Elsayed S. *Raoultella planticola* bacteraemia. J Med Microbiol **61**: 1488-1489, 2012.
18. Demiray T, Koroglu M, Ozbek A, Altindis M. A rare cause of infection, *Raoultella planticola*: emerging threat and new reservoir for carbapenem resistance. Infection **44**: 713-717, 2016.
19. Cho YJ, Jung EJ, Seong JS, et al. A case of pneumonia caused by *Raoultella planticola*. Tuberc Respir Dis **79**: 42-45, 2016.
20. Schlegel L, Grimont F, Ageron E, Grimont PA, Bouvet A. Reap-

praisal of the taxonomy of the *Streptococcus bovis*/*Streptococcus equinus* complex and related species: description of *Streptococcus gallolyticus* subsp. *gallolyticus* subsp. nov., *S. gallolyticus* subsp. *macedonicus* subsp. nov. and *S. gallolyticus* subsp. *pasteurianus* subsp. nov. Int J Syst Evol Microbiol **53**: 631-645, 2003.

21. Corredoira-Sánchez J, García-Garrote F, Rabuñal R, et al. Association between bacteremia due to *Streptococcus gallolyticus* subsp. *gallolyticus* (*Streptococcus bovis* I) and colorectal neoplasia: a case-control study. Clin Infect Dis **55**: 491-496, 2012.

22. Corredoira J, García-País MJ, Coira A, et al. Differences between endocarditis caused by *Streptococcus bovis* and *Enterococcus* spp. and their association with colorectal cancer. Eur J Clin Microbiol Infect Dis **34**: 1657-1665, 2015.

23. Corredoira J, Grau I, Garcia-Rodriguez JF, et al. Colorectal neoplasm in cases of *Clostridium septicum* and *Streptococcus gallolyticus* subsp. *gallolyticus* bacteraemia. Eur J Intern Med **41**: 68-73, 2017.

24. Lee JH, Choi WS, Kang SH, et al. A case of severe cholangitis caused by *Raoultella planticola* in a patient with pancreatic cancer. Infect Chemother **44**: 210-212, 2012.

25. Gözmen S, Şükran Gözmen K, Apa H, et al. Secondary bacteremia in rotavirus gastroenteritis. Pediatr Infect Dis J **33**: 775-777, 2014.

26. Sitaula S, Shahrrava A, Al Zoubi M, Malow J. The first case report of *Raoultella planticola* liver abscess. IDCases **5**: 69-71, 2016.