RAOULETTA PLANTICOLA BACTEREMIA IN A PATIENT WITH EARLY GaSTRIC CANCER

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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

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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°C; 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 (9.1×10⁴/μL) and elevated levels of C-reactive protein (26.3 mg/dL), aspartate transaminase (233 U/L),
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.

Upper gastrointestinal endoscopy was performed for screening purposes, because most patients with \textit{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 \textit{Helicobacter pylori} infection, and the specimen was negative for IgG antibody to \textit{H. pylori}. He was referred to another hospital that specialized in gastroenterology for further examinations and treatment.

**Table 1.** Laboratory Data on Admission.

| Parameter               | Value     |
|-------------------------|-----------|
| Leukocytes (x10^9/μL)   | 7.0 (3.7 - 7.0) |
| Neutrophils (%)         | 85.9 (41.6 - 68.2) |
| Eosinophils (%)         | 0 (0.1 - 4.2) |
| Basophils (%)           | 0.4 (0 - 1.0) |
| Monocytes (%)           | 8.4 (4.9 - 9.7) |
| Lymphocytes (%)         | 5.2 (23.1 - 44.7) |
| Hemoglobin (g/dL)       | 14.6 (14.1 - 17.0) |
| Platelets (x10^9/L)     | 9.1 (15.9 - 30.0) |
| CRP (mg/dL)             | 26.3 (<0.2) |
| CK (U/L)                | 3,278 (62 - 287) |

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 \textit{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          |
| Cefazidine                   | S              | ≤4          |
| Cefmetazole                  | S              | ≤16         |
| Ceftriazone                  | 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

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

Table 3. Reported Cases of R. planticola Bacteremia.

| Reference | Age / Sex | Comorbidities | 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 pipercillin / tazobactam | Recovered |
| 17        | 59 / M    | Pancreatic carcinoma | ERCP | Piperacillin / tazobactam | Recovered |
| 24        | 75 / M    | Pancreatic carcinoma | N/A | Cefotaxime and meropenidazole | 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 meropenidazole | Recovered |
| 13        | 57 / M*   | Non-small-cell lung cancer with multigorgan metastasis | N/A | Levofoxacin, gentamicin, and cefazidime | Recovered |
| 14        | 56 / F*   | Non-small-cell lung cancer with liver metastases | N/A | Ceftriaxone and meropenidazole | 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 levofoxacin | Recovered |
| 15        | 72 / M    | Hepatocellular carcinoma | N/A | No treatment | Died |
| 15        | 59 / M*   | Multiple myeloma | N/A | Cefepime and meropenidazole | 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 meropenidazole | Recovered |
| 15        | 78 / F*   | Cholangiocarcinoma | N/A | Ceftriaxone and meropenidazole | Recovered |
| 15        | 53 / F*   | Gallbladder adenocarcinoma | N/A | Ceftriaxone and meropenidazole | Recovered |
| 15        | 65 / M*   | Pancreatic adenocarcinoma | N/A | Ceftriaxone and meropenidazole | Recovered |
| 15        | 69 / F    | Non-specific | N/A | Ceftriaxone and meropenidazole | 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
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* bio-type 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 a 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).

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