Raoultella ornithinolytica Bacteremia in Cancer Patients: Report of Three Cases

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Abstract

Raoultella ornithinolytica is a Gram-negative aerobic bacillus reclassified in the new genus from the Klebsiella species based on new genetic approaches; however, human infections caused by R. ornithinolytica are rare. We herein report three cases of R. ornithinolytica bacteremia associated with biliary tract infections in cancer patients. R. ornithinolytica can be a causative pathogen of biliary tract infection in cancer patients.

Key words: Raoultella ornithinolytica, bacteremia, biliary tract infection, histamine-producing bacteremia

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Introduction

Raoultella ornithinolytica (R. ornithinolytica) is an encapsulated Gram-negative aerobic bacillus belonging to the Enterobacteriaceae family that was reclassified from the Klebsiella species based on new genetic approaches (1). It is found in aquatic environments, fish and ticks (2) and is a histamine-producing bacterium that is known to cause fish poisoning (3). However, human infections with bacteremia caused by R. ornithinolytica are extremely rare, with only two case reports, including one of bacteremia related to enteric fever syndrome (2) and one of an infant with visceral heterotaxy (4), being reported in the literature. No cases of bacteremia occurring in cancer patients have yet been reported. We herein report three cases of R. ornithinolytica bacteremia associated with biliary tract infections in cancer patients.

Case Reports

We extracted the data for all patients with culture-proven R. ornithinolytica bacteremia diagnosed between January 2005 and December 2011 at Shizuoka Cancer Center, a 569-bed tertiary-care hospital in Japan. A total of three patients fulfilled our inclusion criteria.
Alert 3D system (Sysmex bioMérieux, Tokyo, Japan). Identification of the bacterial species performed with the MicroScan WalkAway 40 plus system (Siemens Healthcare Diagnostics, Tokyo, Japan) classified the bacterium as *R. ornithinolytica*, biotype 77755370, at a probability level of 99.37%.

The isolate of *R. ornithinolytica* exhibited susceptibility to piperacillin, amoxicillin/clavulanate, piperacillin/tazobactam, ceftiraxone, cefazidime, cefepime, meropenem, gentamicin, levofloxacin, minocycline and trimethoprim/sulfamethoxazole; however, it was resistant to ampicillin. The patient was treated with piperacillin/tazobactam for two weeks. Four days after hospitalization, he showed clinical improvements, and the laboratory data returned to normal ranges by day 7. The patient was thereafter transferred to the palliative care unit.

**Case 2**

A 52-year-old woman with advanced-stage pancreatic cancer developing postcholecystectomy was admitted to our hospital with fever and chills. On the day of admission, she was transported to our emergency department by ambulance with a fever, shaking chills and consciousness disturbance. On physical examination, the patient’s blood pressure was 104/60 mmHg, the pulse was 115 beats per minute, the temperature was 39.5°C, the respiratory rate was 28 breaths per minute and the oxygen saturation was 97% on ambient air. The patient’s abdomen was distended but soft, and liver knock pain was positive. The laboratory data obtained on admission revealed a white blood cell count of 13,480/μL with 89% neutrophils, a hemoglobin level of 7.2 mg/dL and a platelet count of 54,000/μL. A serum chemistry analysis with an aspartate aminotransferase level of 3194, an alkaline phosphatase level of 994 IU/L, a total bilirubin level of 2.2 mg/dL, a lactate dehydrogenase level of 388 IU/L and a C-reactive protein level of 19.2 mg/dL. The results of a urinalysis were normal. Blood cultures were obtained and the patient was started on imipenem/cilastatin at a dose of 0.5 g administered every six hours for 104 hours because of a Gram-negative bacillus was isolated, which was identified as *R. ornithinolytica*. The *R. ornithinolytica* isolate exhibited susceptibility to piperacillin, amoxicillin/clavulanate, piperacillin/tazobactam, ceftiraxone, cefazidime, cefepime, meropenem, gentamicin, levofloxacin, minocycline and trimethoprim/sulfamethoxazole; however, it was resistant to ampicillin. Contrast-enhanced abdominal computed tomography was performed, which revealed a low-density area possibly suggestive of a liver abscess or a biloma with biliary duct dilatation. On day 3, percutaneous transhepatic abscess drainage was performed based on a clinical diagnosis of a liver abscess with bacterial cholangitis related to cancerous obstruction of the bile duct; however, the final diagnosis was biloma and a culture of the bile was negative. On day 6, we attempted to perform de-escalation, and it was essential to cover anaerobes in order to prevent any intra-abdominal infection. The antimicrobial therapy was changed to ceftazidime administered at 1 g every six hours for an additional nine days because *R. ornithinolytica* is resistant to ampicillin. The patient thereafter demonstrated a satisfactory improvement.

**Case 3**

A 59-year-old man with gastric cancer presented with fever and chills on postoperative day 5. He was diagnosed as having early-stage gastric cancer and had undergone distal gastrectomy five days earlier. His immediate postoperative course was uneventful; however, on postoperative day 5, he developed fever with chills and right upper abdominal pain. On physical examination, the patient’s blood pressure was 104/65 mmHg, the pulse was 98 beats per minute, the temperature was 38.0°C, the respiratory rate was 16 breaths per minute and the oxygen saturation was 98% while on ambient air. His abdomen was distended but soft, and liver knock pain was positive. The surgical wound was clear. The laboratory data obtained on postoperative day 5 revealed a white blood cell count of 8,140/μL with 94% neutrophils, a hemoglobin level of 12.3 mg/dL and a platelet count of 142,000/μL. A serum chemistry analysis revealed an aspartate aminotransferase level of 44 IU/L, an alanine aminotransferase level of 34 IU/L, an alkaline phosphatase level of 994 IU/L, a total bilirubin level of 1.2 mg/dL, a lactate dehydrogenase level of 247 IU/L and a C-reactive protein level of 6.9 mg/dL. The results of a urinalysis were normal. Specimens for blood culture were obtained and the patient was started on treatment with imipenem/cilastatin at a dose of 4.5 g administered every six hours under a diagnosis of bacterial cholangitis based on the symptoms and elevation of hepatobiliary enzymes. On postoperative day 6, the blood cultures became positive and a Gram-negative bacillus was isolated, which was identified as *R. ornithinolytica*. The *R. ornithinolytica* isolate exhibited susceptibility to piperacillin, amoxicillin/clavulanate, piperacillin/tazobactam, ceftiraxone, cefazidime, cefepime, meropenem, gentamicin, levofloxacin, minocycline and trimethoprim/sulfamethoxazole. We attempted to perform de-escalation, and it was vital to cover anaerobes since the diagnosis was bacterial cholangitis. The antimicrobial therapy was changed to ceftazidime administered at 1 g every six hours because *R. ornithinolytica* is resistant to ampicillin. The patient showed a clinical improvement in the symptoms. The antibiotics were administered via the intravenous route for seven days and changed to oral amoxicillin/clavulanate at a dose of 500 mg/125 mg administered three times daily for an additional seven days.

**Discussion**

*R. ornithinolytica* is a Gram-negative aerobic bacillus belonging to the *Enterobacteriaceae* family. The organism was originally identified as a member of the *Klebsiella* genus, a
member of the family Enterobacteriaceae (1). Klebsiella pneumoniae and K. oxytoca were originally the best known histamine-producing bacteria in fish because prior to 1989, commercial biochemical identification systems were only able to identify histamine-producing strains of Klebsiella pneumoniae and K. oxytoca. In 1989, Sakazaki et al. described the histamine-producing ornithine-positive Klebsiella oxytoca and renamed it ‘Klebsiella ornithinolytica’ (5). In 2001, the genus Raoultella was created based on the analysis of the sequences of the 16S rRNA and rpoB genes from K. ornithinolytica, K. planticola and K. terrigena (6). Kanki et al. concluded that R. ornithinolytica strains and R. planticola are isolated at high frequencies from raw fish and have always been the most important histamine-producing bacteria causing histamine poisoning, so-called ‘Scombroid Fish Poisoning’ (3). With respect to antibiotic susceptibility, R. ornithinolytica has been known to be resistant to ampicillin (7), similar to our findings, and produces chromosomally-encoded class A beta-lactamases (8).

Raoultella spp. infrequently causes human infections; however, R. ornithinolytica has been shown to have the potential to infect human beings. To the best of our knowledge, there are only four cases of human infection reported in the literature. These cases include an 82-year-old woman who presented with intestinal obstruction caused by a giant cyst with a cyst culture showing positive results (9), an infant with bacteremia manifesting as generalized skin flushing with visceral heterotaxy (3) and a 44-year-old woman with a diabetic foot infection presenting with maculopapular rashes related to the histamine-producing characteristics of R. ornithinolytica (10). Our cases, Case 1 and Case 2 were cases of advanced gastrointestinal cancer suspected to involve acute cholangitis. The patient of Case 3 was in a postoperative state after undergoing distal gastrectomy. All of the patients presented with fever and shaking chills with elevated hepatobiliary enzymes and jaundice, and, in all cases, the final clinical diagnosis was biliary tract infection with bacteremia without any findings of rashes related to histamine reactions. The relationship between R. ornithinolytica and biliary tract infection in cancer patients is unclear; however, previous reports of histamine-producing Klebsiella pneumoniae and K. oxytoca were misidentified by less sophisticated commercial systems. Further studies are needed to describe the characteristics of R. ornithinolytica.

In conclusion, we herein reported three cases of R. ornithinolytica bacteremia associated with biliary tract infections in cancer patients. R. ornithinolytica can be a causative pathogen of biliary tract infection in immunocompromised or postsurgical patients, especially those with underlying cancer.

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

References


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