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Case Report

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Source Investigation and Control of *Ralstonia mannitolilytica* Bacteremia in a Neonatal Intensive Care Unit: A Case Report

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ABSTRACT

A case of persistent *Ralstonia mannitolilytica* bacteremia in the neonatal intensive care unit prompted source investigation due to its rarity. After an extensive investigation, a contaminated ultrasonic nebulizer was identified as the source, and the infection was controlled by removing the source. This study emphasizes the importance of further investigations, even in single cases of rare pathogens.

Keywords: *Ralstonia mannitolilytica*; Infection control; Healthcare associated infection; Neonatal intensive care unit

INTRODUCTION

Ralstonia mannitolilytica is a gram-negative, non-fermenting bacterium prevalent in various sources of water supply.[1-3] Although a rare pathogen,[4] *R. mannitolilytica* is an emerging opportunistic pathogen in hospital settings. It causes infections, such as osteomyelitis, meningitis, and bacteremia, with varying degrees of severity, which can in turn lead to sepsis.[2,3,5,6]

An outbreak is generally defined as a sudden increase in the observed number of cases of a disease compared to the expected number in a specific group of individuals over a particular period of time.[7] In general, an infection outbreak or cluster of cases prompt further source investigation; however, a single case of a rare pathogen may also necessitate investigation. Herein, we present a case of persistent bacteremia with *R. mannitolilytica,* which prompted further investigation due to its rarity in the neonatal intensive care unit (NICU). This study was reviewed and approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (IRB No. B-1910-572-702).

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No potential conflict of interest relevant to this article was reported.

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CASE

A 39-day old male infant admitted to the NICU was referred to our hospital's pediatric infectious diseases division for antibiotic treatment of *R. mannitolilytica* bacteremia. The infant was born at a gestational age of 38 weeks 6 days with a birth weight of 2,770 g through normal vaginal delivery, and was admitted to the NICU, comprising 40 beds. The patient was administered prostaglandin E1 (PGE1) through a peripherally inserted central venous catheter (PCVC) immediately after birth due to underlying heart anomalies, D-transposition of the great arteries, ventricular septal defect, and pulmonary atresia. Due to the underlying heart condition, the patient had respiratory distress and was provided respiratory support with a high-flow nasal cannula.

On day seven of admission, the patient developed a fever of up to 38.3°C. Complete blood cell count, C-reactive protein (CRP) level, peripheral blood culture, and chest radiography showed no signs of infection. The patient continued having intermittent mild fever of up to 38.2°C at an interval of 24–48 hours. Complete physical examination, blood tests, peripheral blood cultures, and chest radiography were performed every two to three days; however, all the findings were negative. Because there were no signs of infection, the fever was considered to be PGE1-related.

On day 34 of admission, the patient's body temperature increased to 39.2°C. Systolic and diastolic blood pressures were 81 mmHg and 39 mmHg, respectively; heart rate, respiratory rate, and oxygen saturation were 186/min, 56/min and 83%, respectively. Before the new onset of high fever, the patient had been on respiration support with a high-flow nasal cannula with supplemental oxygen. After the development of the high fever, the patient's respiratory status did not change significantly. Laboratory findings revealed a white blood cell count of 9,500/μL, hemoglobin of 11.7 g/dL, hematocrit of 36.5%, platelet count of 334,000/μL, and CRP protein increased to 9.04 mg/dL. Chest radiography showed no infiltration in either lung fields.

After peripheral blood cultures were obtained, piperacillin/tazobactam was initiated for empirical treatment. A spinal tap was performed, and there was no evidence of central nervous system infection. Gram-negative bacilli growth was reported on an initial blood culture after two days (day 36 of admission). A follow-up peripheral blood culture was performed, and his antibiotics were changed to meropenem. *R. mannitolilytica* was persistently isolated from three serial peripheral blood cultures performed 48 hours apart. The PCVC was removed five days after the first blood culture was positive, and all identified bacteria were sensitive to ciprofloxacin, imipenem, trimethoprim/sulfamethoxazole, piperacillin/tazobactam, ceftriaxone, and tetracycline and resistant to amikacin, aztreonam, ceftazidime, gentamicin, tobramycin, colistin, meropenem, amoxicillin/clavulanic acid, ampicillin, cefazolin, cephalexin, ertapenem, and nitrofurantoin. Based on the antibiotic susceptibility profile, the antibiotic was changed to ceftriaxone (**Table 1**).

Due to prolonged bacteremia, defined as bacteremia over five days after initiation of susceptible antibiotics, imaging studies were performed to evaluate the focal infection sites. Echocardiography showed findings concordant with known underlying heart disease without thrombus or vegetation around the valves. Abdominal ultrasonography showed no abnormal findings in the liver, spleen, gall bladder, pancreas, or bowel. Brain ultrasonography results were also normal. Five days after the first bacteremia occurred (day 39 of admission),

Table 1. Antibiotic susceptibility testing of *Ralstonia mannitolilytica*

Antibiotic	Susceptibility
Amikacin	R
Aztreonam	R
Ceftazidime	R
Ciprofloxacin	S
Gentamicin	R
Imipenem	S
Tobramycin	R
Trimethoprim/Sulfamethoxazole	S
Piperacillin/Tazobactam	S
Colistin	R
Meropenem	R
Ceftriaxone	S
Tetracycline	S
Amoxicillin/Clavulanic-acid	R
Ampicillin	R
Cefazolin	R
Cefoxitin	R
Cephalexin	R
Ertapenem	R
Nitrofurantoin	R

Abbreviations: R, resistant; S, susceptible.

the patient's oxygen saturation dropped to 61%, and chest radiography showed signs of pneumonia with infiltrations in the right upper and both lower lobes. With a sudden increase in the need for further respiratory support, the patient was intubated with an endotracheal tube and mechanical ventilation was initiated.

In consideration that *R. mannitolilytica* had not been detected in the NICU of our institution before, the patient had persistent *R. mannitolilytica* bacteremia and was clinically deteriorating with newly developed pneumonia, environmental investigation was initiated and surveillance culture for medical devices applied to the patient was performed. Transtracheal aspirate cultures detected no bacteria. However, *R. mannitolilytica* was detected in four surveillance cultures, all from the three ultrasonic nebulizers in the NICU, 3 from the drainage tubes of each device, and 1 from an oscillator. The ultrasonic nebulizer was found to have been applied to the patient as a humidifier to decrease the patient's body temperature from day seven of admission, when the fever developed.

After removing the contaminated device, *R. mannitolilytica* was no longer detected in blood cultures on day 6 after the first bacteremia event (day 40 of admission). Body temperature returned to normal on day 41 after admission. Serial chest radiography revealed an improvement in pneumonia. Ceftriaxone was administered for another 14 days after blood culture showed negative conversion. The patient underwent cardiac surgery on day 51 of admission because his general condition and vital signs stabilized without any signs of infection. He was discharged from the NICU on day 94 of admission without complications, such as endocarditis, osteoarticular infection, or other invasive bacterial infections (**Fig. 1**).

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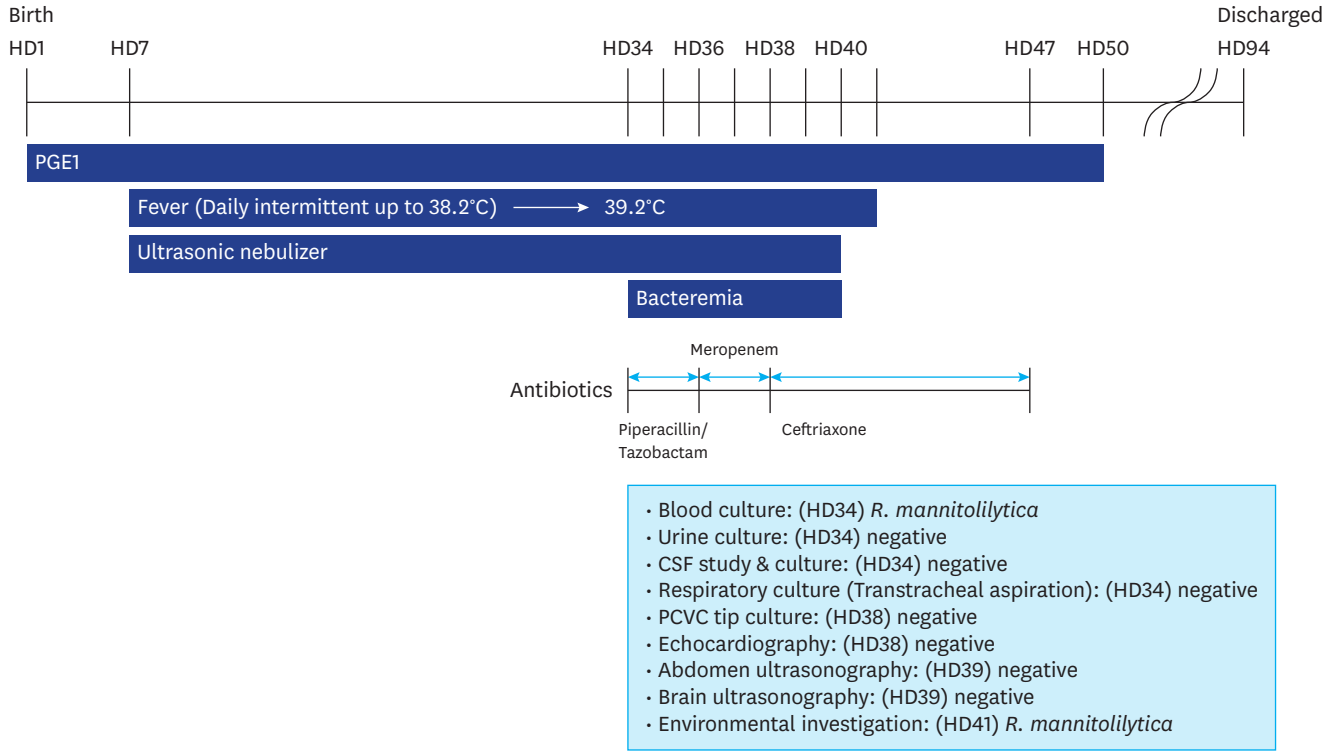

Fig. 1. Clinical course and source investigation.
Gray bars indicate duration of PEG1 use, fever, humidifier use and bacteremia. All the investigations carried out are listed in a box.
Abbreviations: PGE1, prostaglandin E1; HD, hospital day; CSF, cerebrospinal fluid; PCVC, peripherally inserted central venous catheter.

DISCUSSION

In this case report, we have reported on a source investigation of a rare case of *R. mannitolilytica* bacteremia due to exposure to a contaminated ultrasonic nebulizer. Environmental investigation was initiated due to the rarity of *R. mannitolilytica* infections, especially in the NICU, and persistence of bacteremia in the absence of focal infection.

R. mannitolilytica infections associated with contaminated medical equipment have been reported. In the United States, the Vapotherm oxygen delivery device caused an outbreak of *R. mannitolilytica* infection among pediatric patients in 2005.[2,8] In 2007, Gröbner et al.[4] reported multiple cases of central venous catheter-related *R. mannitolilytica* bacteremia among patients with haemato-oncologic diseases, which was suggested to be associated with contaminated intravenous solutions. Such phenomena may occur because *Ralstonia* species survive well in liquid media and hospital devices, owing to their ability to produce biofilms and their low nutritional needs.[1-3,5] These traits also allow them to acquire frequent antibiotic resistance, evade the immune response of patients, and show disinfectant resistance, as they can survive even in chlorhexidine solutions.[3,5,6]

Because there was no source of infection in the patient, potential environmental sources were investigated. Three ultrasonic nebulizers were used in the NICU, and 1 nebulizer (number 2) was used for our patient. Although *R. mannitolilytica* was not isolated from the oscillator, the cup containing vapor solution, the cover of the cup, or the circuit that delivers vapor to the

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patient, it was isolated from the drainage tube of nebulizer number 2. Surveillance cultures of the other 2 ultrasonic nebulizers (numbers 1 and 3) also detected *R. mannitolilytica* in their oscillators and drainage tubes.

Ultrasonic nebulizers were used alternatively as humidifiers to decrease the patient's body temperature. Such unusual applications of ultrasonic nebulizers are not routinely performed in the NICU. However, in this case, because the patient suffered from persistent febrile conditions, nebulizers were used for a different purpose instead of their original purpose. The use of the ultrasonic nebulizers was banned from the NICU because they were the infection sources in the current case and could be potential infection sources in the future. After removing the infection source, the bacteremia was effectively controlled.

This case highlights the importance of thorough investigation of an infection source, especially in infections caused by new or rare pathogens. Furthermore, in cases where bacteremia persists despite appropriate antibiotic therapy without definite infection foci, investigating potential environmental sources may be necessary. This case emphasizes the importance of monitoring the use and management of medical devices in various departments throughout the hospital for infection prevention and control.

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요약

*Ralstonia mannitolilytica*는 다양한 종류의 상수도에 퍼져 있는 그람 음성세균으로써 병원체로는 흔하지 않지만 골수염, 수막염, 균혈증, 패혈증 등 심각한 결과를 초래하는 기회감염을 일으킬 수 있다. 저자들은 신생아 중환자실에서 발생한 *R. mannitolilytica* bacteremia 단일 사례를 보고한다. 재태주수 38주 6일에 2,770 g으로 출생한 환아는 대혈관전위, 심실중격결손, 폐동맥협착이 있어 신생아 중환자실로 입실해 프로스타글란딘E1을 투약 받았으며, 생후 7일부터 간헐적으로 발열이 있어 감염을 배제한 후 체온을 낮추기 위해 가습기를 사용하였다. 생후 34일에 39.2℃ 의 고열이 있어 시행한 혈액배양 검사에서 *R. mannitolilytica*가 동정되었다. 이전에 *R. mannitolilytica*가 기관에서 검출된 적이 없었을뿐더러 항생제 치료에도 균혈증이 지속되어 환경 조사 및 의료기기에 대한 감시 배양를 시행하였다. 환아에게 사용한 가습기에서 *R. mannitolilytica*가 동정되었고, 가습기 사용을 중단한 후로 균혈증, 발열이 호전되었다. 이 증례는 새로운 또는 흔하지 않은 감염이 있을 경우 감염원에 대한 면밀한 조사가 중요함과 적절한 항생제 치료에도 반응이 없을 경우 환경조사가 필요함을 시사한다.

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