Case Report
https://doi.org/10.3947/ic.2017.49.3.227
Infect Chemother 2017;49(3):227-229
ISSN 2093-2340 (Print) · ISSN 2092-6448 (Online)

ic Infection & Chemotherapy

MALDI-TOF-MS Fingerprinting Provides Evidence of Urosepsis caused by *Aerococcus urinae*

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Urosepsis due to *Aerococcus urinae* is rare in clinical settings with only a few of reported cases worldwide by 16S rRNA sequencing. Here we report a case of sepsis caused by *A. urinae* in a 86 year-old male with complicated urinary tract infection which was confirmed through peptide mass fingerprinting of matrix-assisted laser desorption ionization time of flight mass spectrometry.

Key Words: Urosepsis; *Aerococcus urinae*; Matrix-assisted laser desorption ionization time of flight mass spectrometry

Introduction

Urosepsis is defined as sepsis caused by a urogenital tract infection (UTI), which accounts for approximately 25% of all sepsis cases in adults, and most cases are due to complicated UTIs [1]. The bacterial spectrum in urosepsis is composed of 61% *Escherichia coli*, 16% other *Enterobacteriaceae*, 8% *Staphylococcus aureus* and 6% enterococci [2]. However, if the host immune system is suppressed, less virulent organisms, such as enterococci, coagulase- negative staphylococci or *Pseudomonas aeruginosa*, can cause urosepsis.

Aerococcus urinae is known to colonize the human urinary tract and may cause symptomatic UTI [3], infective endocarditis [4] and bacteremia [5]. However, sepsis due to UTI by *A. urinae* is not commonly recognized in clinical settings and inadequate treatment of this infection has been linked to fatal outcomes and severe complications [6]. Here, we report a case of urosepsis due to *A. urinae* identified through matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF-MS).

Case Report

An 86-year-old man was admitted to the hospital with both feet edema and generalized weakness of 15 days with elevated creatinine, suggesting the acute aggravation of chronic renal failure. He also had diabetes mellitus for more than 10 years and history of treated prostate cancer. On day 2 of hospitalization his fever spiked to 38.1℃ and blood and urine cultures were drawn. The growth was detected in one anaerobic blood culture bottle (BacT/ALERT, bioMérieux, Marcy-l'Etoile,

Received: May 17, 2016 **Accepted:** June 21, 2016 **Published online:** May 23, 2017
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France) out of three total pairs of blood cultures. Grayish pinpoint-sized alpha-hemolytic colonies grew on blood agar and Gram-positive cocci in clusters were observed on microscopy. His urine culture grew, >10^5 CFU/mL of a similar organism with >10^5 CFU/mL of *E. coli*. The isolates from blood and urine culture were identified as *A. urinae* by the VITEK 2 system GP (Gram-positive) II card (bioMérieux).

16S rRNA gene sequencing and MALDI-TOF-MS (Bruker Daltonik GmbH, Bremen, Germany) further confirmed the identification of the organisms. The 16S rRNA gene sequences of the two isolates were identical to each other (783 bp) and were 99.2% similar to *A. urinae* (GenBank accession no. M778191), differed from *Aerococcus christensenii* (no. Y17005) with 94.1% similarity, and *Aerococcus sanguinicola* (no. AJ276512) with 94.0% similarity in EzTaxon e-database (http://www.ezbiocloud.net/eztaxon). Since the separation between different species was greater than 0.8%, *A. urinae* was considered as acceptable identification [7]. MALDI-TOF-MS analysis yielded isolates from blood and urine by scores of 2.216 and 2.141, respectively on Biotyper 3.1 (Bruker Daltonik GmbH), greater than 2.00, which can be considered an excellent probability for identification. The mass spectrum and peak heights were identical to each other and all m/z difference between two isolates were less than 500 ppm (difference range, 0.063-474.608), which is the limit of mass tolerance (Fig. 1A, B).

The antimicrobial susceptibility of the two isolates was tested according to the disk diffusion interpretive criteria of *Streptococcus* spp. viridans group provided by the Clinical and Laboratory Standards Institute. Both isolates were susceptible to penicillin, ceftriaxone, cefepime, clindamycin, erythromycin, teicoplanin and vancomycin with identical antibiogram.

The patient underwent antimicrobial therapy with ceftriaxone for five days then changed to meropenem after growing of *E. coli* on urine culture. Two days later, teicoplanin was added after growth of *A. urinae* was reported from blood and urine cultures. In the subsequent cultures, *A. urinae* was not detected, he discharged after 19 days of antimicrobial treatment.

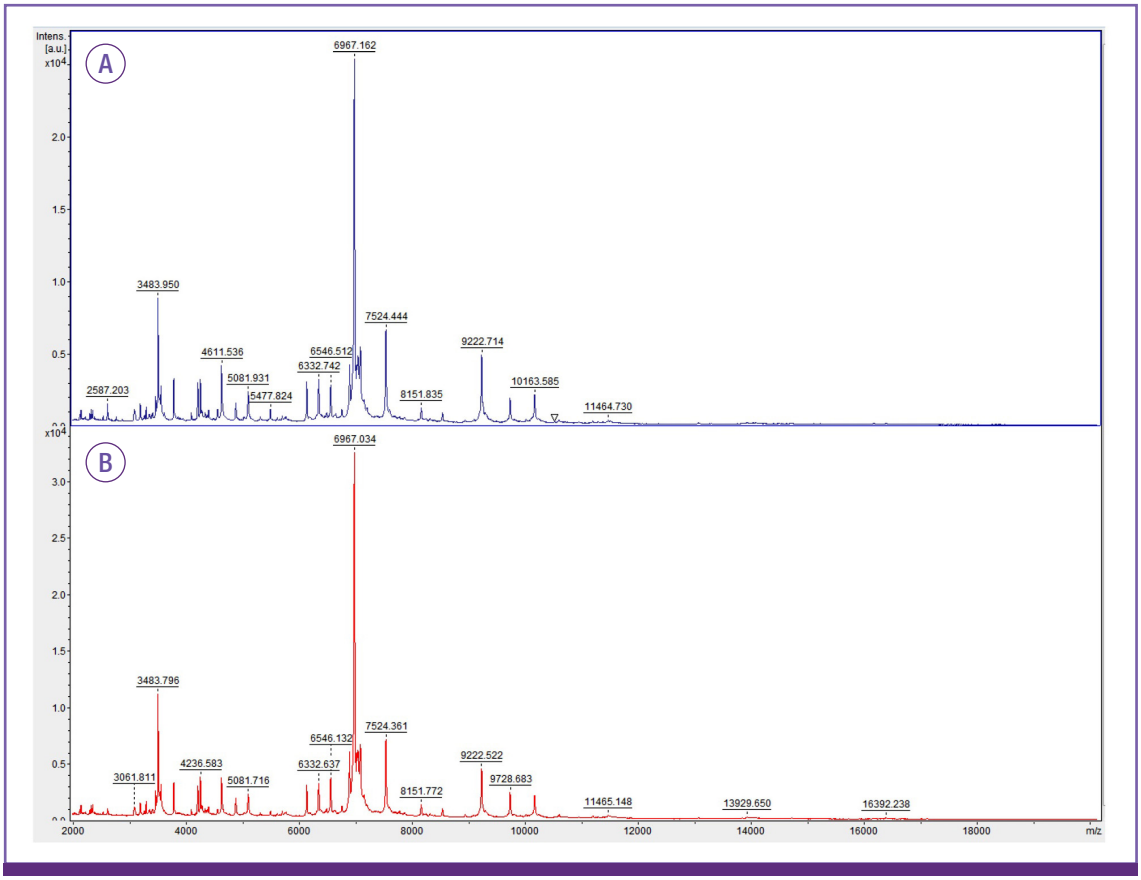

Figure 1. (A) Peptide mass fingerprinting by MALDI-TOF-MS of *Aerococcus urinae* from blood culture; (B) peptide mass fingerprinting by MALDI-TOF-MS of *A. urinae* from urine culture.
MALDI-TOF-MS, matrix-assisted laser desorption ionization time of flight mass spectrometry.

Discussion

A. urinae is facultatively anaerobic, catalase-negative and alpha-hemolytic Gram-positive cocci that forms tetrads and clusters. For its features of both *Staphylococcus* and *Streptococcus*, the secure identification of aerococci has relied on 16S rRNA gene sequencing, however, correct and fast identification is allowed with MALDI-TOF-MS with high sensitivity and specificity [8].

To determine the relatedness of isolates that cause simultaneous infection, genetic typing methods with high discriminatory power are conventionally used, but are time-consuming and cost-intensive. The peptide mass fingerprinting of MALDI-TOF-MS facilitates the identification of clonality rapidly with accuracy and reproducibility, and therefore might be used as a definitive tool to track course of infection.

To the best of our knowledge, this report adds a first patient confirmed by MALDI-TOF-MS to the published reports of urosepsis caused by *A. urinae* which were determined by antibiogram [9] or 16S rRNA sequencing [10]. There have been several studies examining the clinical significance of *A. urinae*, but these have not been conclusive, and it is still known as a non-virulent organism which might be able to be treated without antimicrobial treatment [3] or an organism which can cause invasive infection with mortality [6]. However, with the aid of peptide mass fingerprinting by MALDI-TOF-MS, we suggest that *A. urinae* acts as an invasive pathogen, which infected the bloodstream of a patient with a complicated UTI.

Conflicts of Interest

No conflicts of interest.

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