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CASE REPORT

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A Japanese man with community-onset carbapenem-resistant *Stutzerimonas nitrititolerans* bacteremia and a sacral pressure ulcer: a case report

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Abstract

Background *Stutzerimonas* is a recently proposed genus comprising strains formerly classified as *Pseudomonas stutzeri*. The genus includes at least 16 identified species. *Stutzerimonas nitrititolerans*, previously known as *Pseudomonas nitrititolerans*, was initially isolated from a bioreactor. Only one case of human infection has been reported to date, and its pathogenicity remains unknown.

Case presentation We present a case of community-acquired *S. nitrititolerans* bacteremia in a 77-year-old Japanese man with a sacral pressure ulcer. On admission for cerebral infarction, empirical ampicillin/sulbactam was administered because of an infected sacral pressure ulcer. Blood cultures revealed Gram-negative bacilli. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry was unable to identify the species, but 16 S ribosomal RNA gene sequencing identified the isolate NR5426 as *S. nitrititolerans*. Despite negative results for common carbapenem-resistance genes, the strain showed possible metallo-beta-lactamase production. The patient was treated with piperacillin/tazobactam and recovered.

Conclusions This case confirms that *S. nitrititolerans* can cause infection in humans and highlights the antimicrobial susceptibility profile and the treatment strategy for infections caused by this rare bacterium. Further studies are required to determine its resistance mechanisms and the clinical implications.

Keywords *Stutzerimonas nitrititolerans* bacteremia, 16S rRNA sequencing, Non-fermenting Gram-negative bacilli

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Background

Stutzerimonas is a recently proposed genus within the *Pseudomonadaceae* family, comprising strains formerly classified as *Pseudomonas stutzeri*. Currently, *Stutzerimonas* comprises at least 16 named species [1]. In 2019, *Stutzerimonas nitrititolerans* was isolated from a nitrification/denitrification bioreactor and initially named *Pseudomonas nitrititolerans* [2]. The pathogenicity of *S. nitrititolerans* in humans is unclear. To our knowledge, only one human case of *S. nitrititolerans* infection has been reported to date, isolated from the peritoneal dialysis fluid of a patient with chronic renal failure in 2024 [3]. Herein, we present a case of community-acquired *S. nitrititolerans* bacteremia associated with a sacral pressure ulcer and focus on the clinical course and antimicrobial susceptibility.

Case presentation

A 77-year-old Japanese man with no medical history of note was admitted to our hospital due to a cerebral infarction. On admission, he presented with left hemiplegia and an altered mental state, with a Glasgow Coma Scale score of 12 (E4V4M4). His vital signs were temperature: 36.3℃; pulse rate: 107 beats/min; blood pressure: 192/124 mmHg; respiratory rate: 24 breaths/min; and percutaneous oxygen saturation: 93% breathing ambient air. Additionally, he also had a sacral pressure ulcer with redness, swelling, and a foul odor, likely due to prolonged immobility at home for several days. Blood tests revealed elevated C-reactive protein (10.8 mg/dL) and blood urea nitrogen (48.2 mg/dL) levels, and abnormal electrolyte levels (sodium 154 mEq/L, chloride 112 mEq/L), whereas his liver enzyme and creatinine levels were within the normal range. Hematology revealed leukocytosis, with a white blood cell count of 14,200 cells/μL and a neutrophil proportion of 87.2%. He had no history of exposure to antimicrobial agents, animals, marine products, or plants. On admission blood samples were collected for culture before initiating empirical ampicillin/sulbactam (SAM) 3 g intravenously every 6 h for the infection of the sacral pressure ulcer.

Both aerobic blood cultures (BACTEC, Becton Dickinson Diagnostic Instrument Systems, Franklin Lakes, NJ, USA) detected growth after 27.5 h of incubation. Gram staining showed thin, Gram-negative, curved bacilli (Fig. 1A). The isolate (NR5426) showed rough whitish sheathed colonies on 5% sheep blood agar (Kyokuto, Tokyo, Japan) (Fig. 1B), and rough small colonies on desoxycholate-hydrogen sulfide-lactose agar (Kyokuto, Tokyo, Japan) after 18 h of incubation under aerobic conditions at 35℃ (Fig. 1C). Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) (Bruker Japan, Kanagawa, Japan, version 12) was unable to identify the isolate using a single-colony direct smear method. The top-hit strain was *Pseudomonas* sp. with a score value of 2.03.

Therefore, 16 S ribosomal RNA (16 S rRNA) gene sequencing was performed to identify the isolate using a universal primer pair: 27 F (5′-AGAGTTTGATCCTGG CTCAG-3′) and 1492R (5′-GGTTACCTTGTTACGACT T-3′) [4]. The isolate was 99.72% identical (1405/1409 bp) to *Stutzerimonas nitrititolerans* GL14(T) (accession number: MH917718), and 98.72% identical (1391/1409 bp) to *Pseudomonas songnenensis* NEAU-ST5-5(T) (accession number: RFFN01000014) in the EzBioCloud 16 S database (http://www.ezbiocloud.net/eztaxon). Dendrogram analysis performed with MEGA software version 11 using the neighbor-joining method [5] revealed that the most homologous strain was *S. nitrititolerans* (Fig. 2).

Antibiotic-susceptibility testing was performed in parallel with 16 S rRNA sequencing using the automated bacterial susceptibility testing system (MicroScan WalkAway, Beckman Coulter, Tokyo, Japan). The minimum inhibitory concentrations (MICs) of some of the antibiotics, including piperacillin/tazobactam (PTZ), aminoglycosides, and fluoroquinolones, were below the measurable range. In contrast, the MICs of carbapenems (imipenem and meropenem) were above the limits (Table 1). The sodium mercaptoacetic acid double-disk synergy test (SMA-DDST) (SMA, 3 mg/disk; Eiken Chemical Co. Ltd., Tokyo, Japan), performed according to the package insert, was positive, indicating that NR5426 could produce metallo-beta-lactamase (MBL). However, multiplex polymerase chain reaction (PCR) was performed on NR5426 to identify common carbapenem-resistance genes (bla_{IMP}, bla_{VIM}, bla_{NDM}, bla_{KPC}, and $bla_{OXA-48-like}$) using primers reported in the literature [6]. The isolate tested negative for all five carbapenem-resistance genes.

The antibiotics were switched from SAM to PTZ 4.5 g every 6 h immediately after receiving the positive blood culture results, prior to identification of the species and antibiotic-susceptibility testing. Cultures of superficial swabs of the sacral pressure ulcer, collected after SAM initiation, were negative for *S. nitrititolerans*. Sacral debridement was performed, and magnetic resonance imaging showed no evidence of sacral osteomyelitis. The patient's fever rapidly defervesced, and the redness and swelling of the sacral ulcer improved after switching the antibiotics to PTZ. On day 5 of hospitalization, the antibiotic susceptibility results for *S. nitrititolerans* NR5426 were obtained. They indicated that it might be an MBL-producing organism. Therefore, isolation precautions were implemented according to protocols for MBL-producing enterobacteria, and hand hygiene was encouraged in accordance with the WHO guidelines [7]. Because PTZ was clinically effective at that time, it was not changed and was administered for 14 days. The

Fig. 1 (**A** Gram-stained sample of the blood culture showing thin, curved, Gram-negative bacilli (× 1000). (**B**, **C**) Rough whitish sheeted colonies on 5% sheep blood agar (**B**), and rough small colonies on desoxycholate-hydrogen sulfide-lactose agar (**C**)

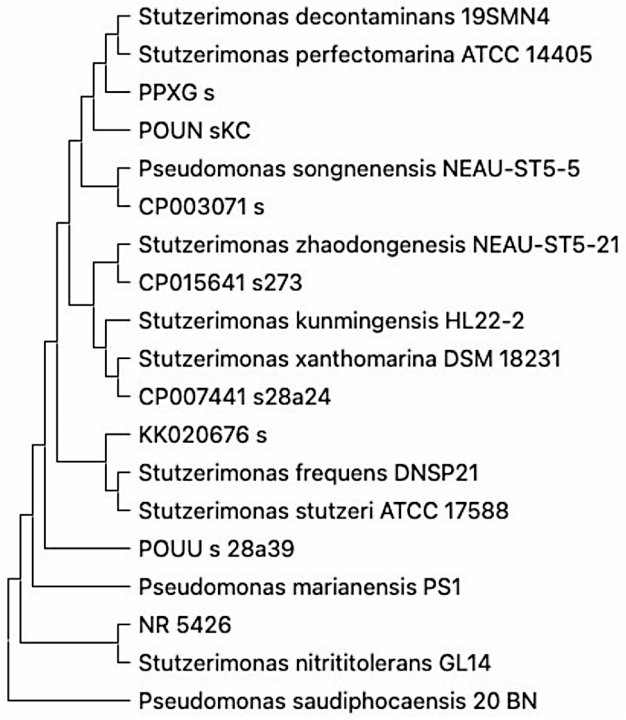

Fig. 2 Phylogenetic tree derived of the 16 S rDNA sequences. The tree was constructed using the neighbor-joining method and nucleotide substitution rate (Knuc) values. The numbers on the tree represent bootstrap values for the branch points, with only values above 50% shown

Table 1 The minimum inhibitory concentrations (MICs) of *Stutzerimonas Nitrititolerans* NR5426

Antibiotic	MIC (μg/mL)
Ampicillin	16
Ampicillin/sulbactam	16/8
Piperacillin	≤ 8
Piperacillin/tazobactam	≤ 8
Cefazolin	> 16
Ceftriaxone	8
Cefepime	≤ 1
Cefmetazole	> 32
Aztreonam	8
Imipenem	> 8
Meropenem	> 8
Gentamicin	≤ 4
Tobramycin	≤ 4
Amikacin	≤ 16
Levofloxacin	≤ 0.12
Ciprofloxacin	≤ 0.25
Minocycline	≤ 1
Trimethoprim sulfamethoxazole	≤ 1/19
Fosfomycin	> 16

*No interpretation of MICs was performed because the Clinical and Laboratory Standards Institute and European Committee on Antimicrobial Susceptibility Testing have not provided breakpoints for *Stutzerimonas nitrititolerans*

patient did not experience recurrence of the pressure ulcer infection after completing the course of PTZ. On day 40 of hospitalization, the patient was transferred to a rehabilitation hospital.

Discussion

The genus *Stutzerimonas*, comprising strains previously classified as belonging to the *Pseudomonas stutzeri* phylogenetic group was proposed as an addition to the *Pseudomonadaceae* family in 2022 (https://lpsn.dsmz.de/genus/stutzerimonas). A PubMed search for "*Stutzerimonas nitrititolerans*" conducted on December 15, 2024, yielded only one article [3]. However, a broader search for bacteremia combined with *S. nitrititolerans* or *P. stutzeri* identified 21 reports, all of which were related to *P. stutzeri*. Additionally, a search for carbapenem-resistant *S. nitrititolerans* or *P. stutzeri* produced 10 relevant results (Additional file). Based on the PubMed searches, only one previous case of human *S. nitrititolerans* infection has been reported to date, described in 2024 [3], and clinical data are limited, raising uncertainty regarding the treatment options. However, several cases of community-acquired or nosocomial infections caused by *Stutzerimonas* spp., specifically *S. stutzeri*, have been reported previously [8–11].

In this case, the patient had a severe infection in the sacral pressure ulcer with *S. nitrititolerans* bacteremia. However, cultures of swabs taken from the site did not grow *S. nitrititolerans*. Because superficial swabs are generally unreliable for diagnosing infections or identifying deep seated microorganisms [12], the cultures from the sacral ulcer were likely inadequate for detecting *S. nitrititolerans*. Given that there was no other obvious infectious source, *S. nitrititolerans* might have entered the blood via the infected sacral pressure ulcer. In previous studies, *S. nitrititolerans* has been isolated from environmental surfaces [1], and *Stutzerimonas* spp. are typically isolated from soil, marine, and hospital environment samples [2, 13]. A previous case report of continuous ambulatory peritoneal dialysis associated peritonitis caused by *S. nitrititolerans* suggests that it was acquired from the medical environment [3]. However, in this case the patient had no history of exposure to soil, marine products, or medical institutions, so how he acquired the bacteria is unclear. However, a retrospective surveillance study of *P. stutzeri* bloodstream infection conducted in Australia during 2000–2019 revealed that 120 of 228 episodes (52.6%) were community-onset and that the most common infectious focus was skin and soft tissue [14]. The incidence was higher in older men, consistent with this case. Given the reclassification of *S. nitrititolerans* from *P. stutzeri*, *S. nitrititolerans* infections could potentially occur in community settings.

S. nitrititolerans NR5426 was resistant to both imipenem and meropenem. *P. stutzeri*, a former classification of *S. nitrititolerans*, is generally susceptible to carbapenems [14–17]. However, some *P. stutzeri* strains have been reported to contain MBL genes such as $bla_{\mathrm{VIM-2}}$ and $bla_{\mathrm{PST-1}}$ [16, 17]. Although no studies on the drug susceptibility of *S. nitrititolerans* have been reported to date, a multidrug-resistant strain, PDI170223, has been identified in ascitic fluid [3]. The isolate demonstrated extended-spectrum β-lactam resistance to piperacillin, third- and fourth-generation cephalosporins (ceftazidime and cefepime), and carbapenems (imipenem and meropenem) [3]. According to the whole-genome sequencing results, *S. nitrititolerans* PDI170223 carried multiple MBL genes, including $bla_{\mathrm{KHM-1}}$, $bla_{\mathrm{IMP-1}}$, $bla_{\mathrm{GIM-1}}$, $bla_{\mathrm{SIM-1}}$, $bla_{\mathrm{VIM-2}}$, and bla_{NDM}. Conversely, *S. nitrititolerans* NR5426 had low MICs for PTZ, ceftazidime, and cefepime, despite demonstrating resistance to imipenem and meropenem. Based on the positive SMA-DDST results, *S. nitrititolerans* NR5426 may also have been MBL-producing, even though multiplex PCR testing to identify bla_{IMP}, bla_{VIM} and bla_{NDM} yielded negative results. Given the effectiveness of PTZ in vivo, *S. nitrititolerans* NR5426 might harbor MBL genes with higher substrate specificity for carbapenems than other β-lactams, which could not be detected by multiplex PCR testing. Other mechanisms involved in carbapenem resistance in Gram-negative bacilli include expression of efflux pumps, alterations in penicillin-binding proteins, and restricted outer-membrane permeability [18, 19]. *S. nitrititolerans* PDI170223 expressed efflux pumps, such as MexAB-OprM and MexEF-OprN [3]. These belong to the RND family with outer-membrane components and relate not only to β-lactam resistance, but also to fluoroquinolone resistance in *Pseudomonas* spp [20]. In this case, *S. nitrititolerans* NR5426 was susceptible to fluoroquinolones, suggesting that upregulation of efflux pumps might not be a key mechanism of carbapenem resistance. Because whole-genome sequencing could not be performed, it is unclear whether gene mutations related to penicillin-binding proteins or decreased permeability of outer-membrane proteins were present. Further investigations are necessary to understand the antibiotic-resistance mechanisms of *S. nitrititolerans*.

Conclusion

We successfully treated a patient with carbapenem-resistant *S. nitrititolerans* NR5426 bacteremia with PTZ. However, the resistance mechanisms remain unclear. This case provides data regarding antimicrobial susceptibility, which could contribute to deciding on antimicrobial treatment of infections caused by this rare bacterium.

Abbreviations

SAM	Ampicillin/sulbactam
MALDI-TOF MS	Matrix-Assisted Laser Desorption Ionization Time-Of-Flight Mass Spectrometry
16S rRNA	16 S ribosomal RNA
MIC	The Minimum Inhibitory Concentration
PTZ	Piperacillin/Tazobactam
SMA-DDST	The Sodium Mercaptoacetic Acid Double-Disk Synergy Test
MBL	Metallo-Beta-Lactamase
PCR	Polymerase Chain Reaction

Supplementary Information

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Supplementary Material 1

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Author contributions

K.H. wrote the main manuscript. K.M. prepared Fig. 1, and Y.O prepared Fig. 2. Y.S and H.Y performed the microbiology examinations.All authors reviewed the manuscript.

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Data availability

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from our patient for publication of this case report and accompanying images in an open access online publication.

Competing interests

The authors declare no competing interests.

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