CASE REPORT

Urinary tract infection by a rare pathogen 
*Cedecea neteri* in a pregnant female with 
Polyhydramnios: rare case report from UAE

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Abstract

**Background:** *Cedecea neteri* is a gram-negative, oxidase-negative bacillus, a rare pathogen. Few reports are emerging globally about its antimicrobial resistance pattern especially in immunocompromised individuals with comorbidities.

**Case presentation:** In this paper, we report the first case of *C. neteri* causing urinary tract infection in a pregnant woman at a specialty care hospital in the Northern Emirates of Ras al Khaimah, UAE.

**Discussion and conclusion:** *C. neteri* is a rare and unusual pathogen, unlike routine gram-negative urinary tract pathogens from the family of *Enterobacteriaceae* and therefore may be missed or misidentified by routine laboratories using conventional microbiology identification techniques. Hence, *Cedecea* infections may be underreported. Physicians and microbiology technicians must be aware of such a rare pathogen, as most of the isolates are multi-drug-resistant and require combined antibiotic treatment with beta-lactamase inhibitors and hence pose a treatment challenge especially in immunocompromised patients with comorbidities. In recent years, it has been reported as an emerging opportunistic pathogen.

**Keywords:** *Cedecea neteri*, Rare pathogen, Urinary tract infection, Multi-drug resistance

Background

*Cedecea neteri* is a gram-negative, oxidase-negative bacillus—a rare pathogen with increasing case reports describing infections by the genus *Cedecea*. However, there have been very few cases of *C. neteri* reported so far, and none from urinary tract infection (UTI). In this paper, we report the first case to the best of our knowledge of *C. neteri* from a 27-year-old, young pregnant female with 35 weeks’ gestation presenting with polyhydramnios.

*Cedecea* constitutes a rare pathogen of increasing importance. *Cedecea* species are known to have antibiotic resistance genes and therefore difficult to treat infections caused by them, due to their broad-spectrum antibiotic resistance. There is emerging literature with case reports of bacteremia caused by *C. neteri* and more cases reported by other *Cedecea* species: *C. davisae* and *C.lapegei*. Nevertheless, the classical case of UTI by *C. neteri* species is rare. Literature review showing case of urinary catheter colonization by multidrug-resistant *C. neteri* in an elderly 88-year-old immunocompromised patient presenting with cellulitis, benign prostatic hyperplasia, and prolong use of Foley’s catheter. The *C.neteri* isolated from urinary catheter was sensitive to most 2nd and 3rd generation cephalosporins and resistant to ampicillin along with β-lactamase inhibitor (Sulbactam) combination, suggesting AmpC β-lactamase production with the presence of multiple metallo β-lactamase genes [1]. In another report from Turkey, described UTI caused by

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Cedecea lapagei in a 40-year male with invasive brain surgery after 3 weeks of rehabilitation and was successfully treated with Ciprofloxacin [2]. Furthermore, there have been emerging reports of the association of C. neteri with other clinical presentations. To mention a few, a report of bacteremia in patients of heart disease [3], in patients with systemic lupus erythematosus [4], and a case report from Saudi Arabia where C. neteri was isolated from peritoneal fluid of an immunocompromised preterm neonate following intestinal perforation due to necrotizing enterocolitis [5]. Infections from Cedecea are mostly reported from immunocompromised patients with multiple comorbidities or invasive procedures, suggesting its role as an emerging opportunistic multi-drug resistant pathogen [1, 3, 5].

Case presentation
Our patient was a 27-year-old pregnant woman at 35 weeks gestation who visited the Gynecology outpatient department of RAK hospital with complaints of increased frequency, urgency, and dysuria; classical presentation of UTI. The patient was on follow-up for polyhydramnios. On examination, she was afebrile, well oriented to time, place, and person, with a pulse rate of 86/min, blood pressure of 152/90 mmHg, a known hypertensive. However, there were no signs of cystitis or pyelonephritis based on abdominal and pelvis ultrasound. Her history revealed that she was multiparous and her first pregnancy ended with twins born by caesarian. During the second pregnancy, she developed polyhydramnios and was on continuous follow-up. Her mid-stream first-morning urine sample macroscopically was cloudy with yellow coloration. Microscopically it showed significant polymorph nuclear cells (18–20 cells/ high power field), no RBCs, and 3+ leukocyte esterase activity with plenty of leukocytes and bacteria with <1 squamous epithelial cell. Culture and identification yielded significant bacteriuria of 10^5 CFU/ml of a gram-negative epithelial cell. Culture and species Cedecea neteri. To confirm the diagnosis of UTI, two mid-stream urine samples on consecutive days were further cultured. Both samples showed significant growth (10^5 CFU/ml) of C. neteri and thus confirmed the diagnosis.

Antimicrobial susceptibility testing showed the isolate to be resistant to Amikacin, Aztreonam, Cefalothin, Ceftiraxone, Ertapenem, Cefepime, Cefoxitin and susceptible to Ampicillin, Ampicloxacin, Nitrofurantoin, Levofloxacin, Tigecycline & Piperacillin/Tazobactum. The patient was treated with one gram of Augmentin (combination of 875 mg amoxicillin and 125 mg clavulanic acid) for 5 days and urine culture was sterile post 1 week of treatment.

Discussion and conclusion
In females, UTI is most often caused by members of the family Enterobacteriaceae mainly E. coli, mostly endogenous, due to the proximity of the anus to the urethra and short urethra causing ascending infections in women. To the best of our knowledge, this is the first case of a UTI by a rare pathogen, Cedecea neteri, reported from the UAE, in a 35-week pregnant, multiparous female who has polyhydramnios and a known case of hypertension. Most likely C. neteri has been a colonic microbial flora of this patient.

Cedecea was described in 1981 as a separate genus of the Enterobacteriaceae family as it was phenotypically distinct from the other members of the family and named after CDC, where the isolates were originally discovered and formerly called as CDC Enteric group 15 [6]. To date, six species of Cedecea have been reported with three species, Cedecea neteri, Cedecea lapagei, and Cedecea davisiæ, that are well characterized. C. neteri is named after the American physician-microbiologist Dr. Erwin Neter [7]. Cedecea species have not been reported to cause invasive infection in healthy individuals, but are considered opportunistic pathogens due to their isolation from severely immunocompromised patients. The case presented here is a pregnant mother who is immunocompromised and therefore more susceptible to infections. The growing fetus also exerts pressure on the urinary bladder, increasing residual urine, thereby affecting complete voiding and urine stasis predisposing to UTI.

These pathogens may be missed or misidentified by routine laboratories using conventional microbiology identification methods and hence may be under-reported. Cedecea neteri strains are gram-negative, rod-shaped, motile [8]. They are characterized by positive biochemical reactions for sucrose, D-sorbitol, and malonate fermentation tests [3, 9]. Clinical history, laboratory diagnosis, and antimicrobial resistance pattern of Cedecea spp. resemble to established pathogen Serratia spp. in terms of lipase positivity and resistance to cephalothin, and colistin (polymyxin E) [3, 7, 8]. C. neteri is distinguished from other Cedecea spp. with negative ornithine decarboxylase activity and its ability to ferment sucrose, D-sorbitol, and D-xylene [3].

Multidrug resistance in Cedecea spp. is attributed to the combination of AmpC production and porin deficiency in the cell wall [8, 10]. However, no definite experimental evidence on this theory is available to this day. Cedecea clinical isolates display variable resistance patterns to major beta-lactam like penicillins, cephalosporins, monobactams, and carbapenems. The latest literature review indicates the highest frequency of
Cedecea spp. resistance to ampicillin (43%), followed by cephalothin (35%), cefoxitin (35%), cefazolin (22%), cef-tazidime from a total of 23 isolates reported to date [11]. Carbapenems and 4th generation cephalosporin resistance may be exhibited in Cedecea isolates harboring metallo-β-lactamase. C. neteri poses another unique feature to enhance its pathogenicity by Quorum sensing activity that has been lately studied in C. neteri strain SSMF04 and can lead to enhanced biofilm formation as well as enhanced antimicrobial resistance [12]. Fortunately, low resistance to fluoroquinolones and no resistance to macrolides have been documented. It is also encouraging to note that most of the reported cases have successful treatment outcomes and an active antibiotic stewardship policy with proactive microbiology laboratory diagnosis and antibiotic sensitivity testing can improve clinical outcomes. C. neteri infections have been reported worldwide, with clinical cases occurring from U.S., Spain, Saudi Arabia, and the latest one from UAE (Table 1. summarizes all the C. neteri cases reported to date).

As summarized in Table 2, most Cedecea infections are reported in immunocompromised patients with underlying medical conditions like uncontrolled diabetes mellitus, chronic kidney disease, liver transplantation, malignancies, chronic obstructive pulmonary disease, and few isolated cases from catheters and central lines, indicating its opportunistic potential and warranting careful attention among these groups of patients.

C. davisae infections have been reported from a broad clinical spectrum with bacteremia as a common clinical presentation. Thirteen cases have been reported to date from different clinical specimens including: 46% from blood, 23% from sputum, urine, cutaneous and oral ulcers, and scrotal abscess. It is also noteworthy that the majority of infections were among patients > 50 years of age with co-morbid conditions.

Apart from the endogenous source of infections from the gut, Cedecea infections are also documented from environmental samples and aquatic habitats. A case report of a patient with minor leg ulcer infection and subsequent bacteremia (Dalmaga et al. 2008) raises concerns of C. davisae infection from lake water.

C. lapagei have been more frequently isolated with pneumonia and bloodstream infections and to date, a total of 11 cases have been reported from blood, sputum, tissue, wound, peritoneal fluid and most patients had co-morbid conditions like acute leukemia, type II diabetes mellitus, pulmonary tuberculosis, liver cirrhosis, and chronic obstructive pulmonary disease. Pediatric infections involving Cedecea are largely associated with C.lapagei, suggesting its role as an uncommon cause of nosocomial pneumonia and sepsis in infants with a history of multiple antibiotic treatment regimens and prolonged hospitalization.

It is also noteworthy, that most of the Cedecea infections are resistant to quinolones (ciprofloxacin, Cefotaxime (third-generation cephalosporin), Imipenem, and Meropenem (carbapenems) and intravenous combination with β-lactamase inhibitors (Piperacillin and Tazobactam) making it a potential multidrug-resistant pathogen. Therefore, clinicians and diagnostic laboratories need to be aware of such rare pathogens that are often drug-resistant and require combined antimicrobial therapy. A complete

| Study year | Patient (age/sex, location) | Cedecea spp | Infection | Diagnosis | Antibiotic Sensitivity/Treatment | Antibiotic Resistance | Clinical Outcome | Reference |
|------------|-----------------------------|-------------|-----------|-----------|---------------------------------|----------------------|-----------------|-----------|
| 2021       | 27/F UAE                     | C. neteri   | Urinary tract infection | Polyhydramnios, hypertension | Amoxicillin and clavulanic acid | Amikacin, Aztreonam, Cephalothin, Ceftriaxone, Ertapenem, Cefepime, Cefoxitin. | Successful recovery | Hafiz et al. 2021 |
| 2018       | 88/M USA                     | C. neteri   | Colonization of the Urinary catheter | Cellulitis, with hypertension, chronic kidney disease and benign prostatic hyperplasia | Cefamandole, cefazidime, ceftriaxone, cefepime, aztreonam, nitrofurantoin, ciprofloxacin, TMP/SMX, Piperacillin/Tazobactam, | Amoxicillin/sulbactam, cefazolin, cefoxitin | Successful recovery | Ginn et al. [1] |
| 2017       | Neonate/M Saudi Arabia       | C. neteri   | Peritonitis | Perforation of Intestine systemic lupus erythematosus | Not reported | Piperacillin/tazobactam and gentamicin | Successful recovery | Arishi et al. [5] |
| 1995       | 27/F Spain                   | C. neteri   | Bacteremia | Intravenous vancomycin, cefazidime, gentamicin | Intravenous vancomycin, cefazidime, ceftriaxone | Amoxicillin, cephalosporins, amoxicillin and clavulanic acid, aminoglycosides | Died | Augieria et al. [4] |
| 1982       | 62/M USA                     | C. neteri   | Bacteremia | Cardiac and valvular heart disease | Cefamandole, chloramphenicol | Cefalothin, ampicillin, colistin | Successful recovery | Farmer et al. [3] |
Table 2 Summary of representative *Cedecea* spp. cases reported to date

| Study year | Patient (age /sex, location) | *Cedecea* spp. | Infection | Diagnosis | Antibiotic Resistance | Treatment | Clinical Outcome | Reference |
|------------|-----------------------------|----------------|-----------|-----------|----------------------|-----------|-----------------|-----------|
| 2019       | Neonate/India               | *C. lapagei*   | Nosocomial Pneumonia | Late preterm | Meropenem, Colistin, amikacin, ceftazidime | Piperacillin/tazobactam | Recovered | Ramaswamy et al. 2019 [13] |
| 2019       | 41/F USA                    | *C. davisae*   | Biliary sepsis | Minimal change disease | Ampicillin, ceftriaxone, cefuroxime | Ciprofloxacin, metronidazole | Recovered | Kanakadandi et al. [10] |
| 2018       | 52/M Mexico                 | *C. lapagei*   | Soft tissue bullae leading to septic shock, Liver cirrhosis, esophageal varices, hypertension | | Ampicillin, cefazolin, imipenem; ampicillin/ sulbactam | Intravenous imipenem, clindamycin | Died | Chavez Herrera et al. 2018 [14] |
| 2017       | Neonate/M Brazil            | *C. lapagei*   | Ventilator-associated pneumonia, sepsis | | Not reported | Multiple courses of antibiotics including meropenem | Recovered | Kury et al. [15] |
| 2017       | Neonate/M India             | *C. lapagei*   | Late-onset sepsis | Preterm | Imipenem, meropenem, aztreonam, ceftazidime, cefotaxime, cefoxitin, cilastatin, piperacillin/tazobactam, | Amoxicillin, cefotaxime | Recovered | Ahmad et al. [16] |
| 2016       | Neonate/F India             | *C. lapagei*   | Neonatal sepsis | Term infant | Amoxicillin/ clavulanic acid, ceftazidime, ceftriaxone, gentamicin, cefuroxime, piperacillin/tazobactam, | Ciprofloxacin, amikacin | Recovered | Islam et al. [17] |
| 2015       | 50/M India                  | *C. lapagei*   | Superinfection of malignant oral ulcer, Squamous cell carcinoma of the right buccal mucosa | | Amoxicillin/sulbactam, tetracycline, tigecycline | Ciprofloxacin, | Recovered | Biswal et al. [18] |
| 2006       | 55/M USA                    | *C. lapagei*   | CAPD-related peritonitis | CAPD, Hypertension, Liver transplantation, cirrhosis, end-stage renal disease | | Initially intravenous vancomycin & gentamicin, followed by ceftazidime & gentamicin added to PD | Recovered | Davis & wall [19] |
| 2012       | 54/M Greece                 | *C. davisae*   | Bacteremia | Stage IV sigmoid colon carcinoma | Tobramycin | Gentamicin | Recovered | Akinosoglou et al. [20] |
| 2012       | 20/M USA                    | *C. davisae*   | Polymicrobial* HCA pneumonia | Cystic Fibrosis | | | Recovered | Ismael et al. [21] |
| 2011       | 52/M USA                    | *C. davisae*   | Central line-related bacteremia | Acute myeloid leukemia, neutropenia, *C. difficile* colitis | Ceftazidine, ciprofloxacin, piperacillin/tazobactam | Imipenem | Recovered | Abate et al. [22] |
| 2008       | 67/M Greece                 | *C. davisae*   | Leg ulcer, bacteremia | Uncomplicated DM | Cefotaxime, cefuroxime, sodium, cefoxitin, | | Recovered | Dalamaga et al. [23] |

**Notes:**
- HCA: Hospital acquired.
- CAPD: Continuous ambulatory peritoneal dialysis.
- β-lactams: B-lactam antibiotics.
antimicrobial susceptibility testing profile, especially with beta-lactam inhibitors is warranted to provide the best treatment options, especially among immunocompromised patients with comorbidities. (Tables 1, 2) The present reported *C. neteri* isolate was resistant to most of the third and fourth generation cephalosporin except a few amino and carboxypenicillins that provided a successful treatment outcome. This report further adds to the existing literature on diagnosis, clinical presentation, antibiotic susceptibility, and clinical management of *C. neteri* infection.

**Abbreviations**
RAK: Ras al Khaimah; UTI: Urinary Tract Infections (UTI); CLED Agar: Cysteine Lactose Electrolyte Deficient Agar; CFU: Colony Forming Unit; CDC: Centers for Disease Control and Prevention; U.A.E: United Arab Emirates

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**Authors’ contributions**
HA: Made substantial contributions from drafting, conception, sample testing, and analysis and writing the Manuscript; TM-Made substantial contributions by managing the patient and providing clinical data and patient follow-up; SAP-Made substantial contributions to the laboratory analysis of the samples obtained. DP: Made substantial contributions to the interpretation of results and manuscript writing and proofreading the revised manuscripts. All authors have read and approved the manuscript.

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**Availability of data and materials**
All patient data is coded and kept confidential under authorization control in the hospital’s Laboratory Information Management System and cannot be shared. However, parts of Cedecea neteri report generated by automated microbiology system can be shared upon request without compromising patient information. The data is user restricted and was accessed by the study PI: Dr. Hafiz Ahmad who is also a clinical microbiologist at the Department of Microbiology at RAK Hospital, Ras al Khaimah, UAE.

**Declarations**

**Ethics approval and consent to participate**
Ethical clearance and approval for the study were obtained from the RAK Medical and Health Sciences university ethical committee, approval letter no: RAKMHSU-REC-055-2019-F-M.

**Consent for publication**
Written and verbal patients consent for clinical sample testing, procedures, and publication for the academic purpose was taken by treating Gynecologist Dr. Talat Masroor at RAK hospital and is recorded electronically in LIMS RAK hospital software.

**Competing interests**
The authors declare that they have no competing interests.

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