CASE REPORT Open Access

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.lapagei. 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 Foleys 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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Ahmad et al. BMC Infectious Diseases (2021) 21:637

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 10⁵ CFU/ml of a gramnegative bacterium grown in Cysteine Lactose Electrolyte Deficient (CLED) agar. On further characterization, the isolate was identified by Phoenix automated microbial identification system (BD Diagnostics, Spars, Maryland), belonging to genus *Cedecea* and species *neteri*. To confirm the diagnosis of UTI, two mid-stream urine samples on consecutive days were further cultured. Both samples showed significant growth (10⁵ CFU/ml) of C. *neteri* and thus confirmed the diagnosis.

Antimicrobial susceptibility testing showed the isolate to be resistant to Amikacin, Aztreonam, Cephalothin, Ceftriaxone, Ertapenem, Cefepime, Cefoxitin and susceptible to Ampicillin, Ampicloxacillin, 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.

Page 2 of 6

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 davisae, 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 underreported. *Cedecea neteri* strains are gram-negative, rodshaped, 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. resemblance 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-xylose [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, monobactam, and carbapenems. The latest literature review indicates the highest frequency of

Ahmad et al. BMC Infectious Diseases (2021) 21:637

Page 3 of 6

Cedecea spp. resistance to ampicillin (43%), followed by cephalothin (35%), cefoxitin (35%), cefazolin (22%), ceftazidime 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.

<u>C.</u> 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 comorbid 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

Table 1 Cases of *Cedecae neteri* reported to date

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	cefmandole, ceftazidime, ceftriaxone, cefepime, aztreonam, nitrofurantoin, ciprofloxacin, TMP/SMX Piperacillin/tazobactam,	Ampicillin/sulbactam, cefazolin, cefoxitin	Successful recovery	Ginn et al. [1]
2017	Neonate/M Saudi Arabia	C. neteri	Peritonitis	Perforation of Intestine	Not reported	Piperacillin/tazobactam and gentamicin	Successful recovery	Arishi et al. [5]
1995	27/F Spain	C. neteri	Bacteremia	systemic lupus erthematosus	Intravenous vancomycin, ceftazidime, gentamicin	Amoxicillin, cephalosporins, amoxicillin and clavulanic acid, aminoglycosides	Died	Augileria et al. [4]
1982	62/M USA	C. neteri	Bacteremia	Cardiac and valvular heart disease	Cefamandole, chloramphenicol, n	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)	· · · · · · · · · · · · · · · · · · ·	Infection	Diagnosis	Antibiotic Resistance	Treatment	Clinical Outcome	Reference
2019	Neonate/ India	C. lapagei	Nosocomial Pneumonia	Late preterm	Meropenem, Colisitin, 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. Iapagei		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. Iapagei	Ventilator- associated pneumonia, sepsis		Not reported	Multiple courses of antibiotics including meropenem	Recovered	Kury et al. [15]
2017	Neonate/M India	C. Iapagei	Late-onset sepsis	Preterm	Imipenem, meropenem, aztreonam, ceftazidime, cefotaxime, cefoxitin, cefepime,	Ampicillin, 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, TMP/SMX	Ciprofloxacin, amikacin	Recovered	Islam et al. [17]
2015	50/M India	C. Iapagei	Superinfection of malignant oral ulcer	Squamous cell carcinoma of the right buccal mucosa	Ampicillin/ 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	Not reported	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	All tested β- lactams, aminoglycosides, fluoroquinolones, tigecycline	TMP/SMX	Recovered	Ismael et al. [21]
2011	52.M USA	C. davisae	Central line- related bacteremia	Acute myeloid leukemia, neutropenia, <i>C. difficile</i> colitis	Ceftazidime, ciprofloxacin, piperacillin/ tazobactam	Imipenem	Recovered	Abate et al. [22]
2008	67/M Greece	C. davisae	Leg ulcer, bacteremeia	Uncomplicated DM	Cephalothin cefuroxime sodium, cefoxitin,	Cefotaxime, amikacin	Recovered	Dalamaga et al. [23]

Ahmad et al. BMC Infectious Diseases (2021) 21:637 Page 5 of 6

Table 2 Summary of representative *Cedecea spp.* cases reported to date *(Continued)*

Study year	Patient (age /sex, location)	Cedecea spp.	Infection	Diagnosis	Antibiotic Resistance	Treatment	Clinical Outcome	Reference
					ampicillin, piperacillin, nitrofurantoin, tetracycline			
2008	47/M Greece	C. Iapagei	Bacteremia and wound infection from cement- related chemical burns	Diabetes mellitus	Gentamicin, Tobramycin, cephalothin, cefoxitin, sodium, cefoxitin, ampicillin, piperacillin, nitrofurantoin, tetracycline	Cefotaxime, amikacin	Recovered	Dalamaga et al. [24]
1983	50/M USA	C. davisae	Scrotal Abscess	Chronic hypertensive cardiac disease, alcoholic hepatitis	Ampicillin, cephalothin, cefamandole, cefoxitin, chloramphenicol	Tetracycline	Recovered	Bae & Sureka [25]

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

Acknowledgments

The author's acknowledge Hospital CEO's - Dr. Raza Siddiqui and Dr. Jean Marc Gauer and RAK Medical & Health Sciences University Dean Dr. KL Bairy and President Dr. S. Gurumadhva Rao for their support to publish the study.

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.

Funding

Non-funded

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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Received: 30 August 2020 Accepted: 9 June 2021 Published online: 02 July 2021

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