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Leclercia adecarboxylata: An Emerging Multidrug Resistant Pathogen Causing Catheter Related Bacteremia with Review of Literature

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Abstract

Leclercia adecarboxylata has been regarded as an opportunistic pathogen that causes infections mainly in immunocompromised patients. Blood stream infections caused by L. adecarboxylata is considered as a complication in patients with indwelling catheters Although L. adecarboxylata has been recognized as a human pathogen with low virulence and high antibiotic susceptibility, there has been emergence of multi-drug resistant strains, leaving behind limited therapeutic options. We report a case of catheter-related bacteremia in a fifty-year-old female with breast carcinoma, caused by extended-spectrum beta-lactamase (ESBL) producing L. adecarboxylata. Rapid and correct identification and timely institution of appropriate antibiotic therapy was the key to favorable clinical outcome in our case.

Keywords: *Leclercia adecarboxylata, Bacteremia, Indwelling catheters, ESBL*

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I. Introduction:

Leclercia adecarboxylata is a peritrichous-flagellated, facultatively anaerobic, Gram-negative bacillus belonging to the pigmented group of Enterobacteriaceae family. *Leclercia adecarboxylata* was formerly designated as Enteric group 41 and *Escherichia adecarboxylata*. It was first identified by a French bacteriologist Leclerc in 1962.[1,2,3] Subsequently, based on nucleic acid and protein electrophoretic techniques, it was separated from the genus *Escherichia*, and renamed as *Leclercia adecarboxylata*.[3,4] It is ubiquitously distributed in nature and has been isolated from soil, water, and other environmental sources. It also inhabits the human gastrointestinal tract.[3,5] It has been recognized as an emerging pathogen, with the potential to cause severe illnesses such as septicaemia, diarrhea, pneumonia, peritonitis, septic arthritis, skin and soft tissue infections, abscesses and urinary tract infection, both in immunocompromised and immunocompetent individuals.[6,7] Various authors across the world have described *L. adecarboxylata* as an opportunistic bacterium causing infections in immunosuppressed patients suffering from primary diseases such as cancer, leukemia, hepatoma, and renal failure.[8-11] Generally, *L. adecarboxylata* is sensitive to most antibiotics; however, extended-spectrum beta-lactamase producing and metallo-beta-lactamase producing strains have also been reported.[12 -15] Stock I et al.[3] documented that strains of *L. adecarboxylata* are naturally resistant to penicillin G, oxacillin, erythromycin, clarithromycin, ketolides, lincosamides, streptogramins, linezolid, glycopeptides, rifampicin and fosfomycin. To the best of our knowledge, bloodstream infection caused by this rare organism has not been reported from this geographical area. We, hereby, report a case of catheter-related bacteremia caused by extended-spectrum beta-lactamase-producing *L. adecarboxylata* in an immunocompromised patient with breast malignancy.

II. Case Report

A fifty-year-old female presented in emergency unit with the chief complaints of high grade fever with chills and rigors since last 3 days, not responding to antipyretics. As per patient's medical records, she was a diagnosed case of right breast carcinoma, had undergone mastectomy about 2 months back. After one month of surgery, she was put on chemotherapeutic agents. Chemotherapy was administered through a peripherally inserted central catheter (PICC) inserted in the left basilic vein. About two weeks, following chemotherapy through

PICC, she developed a high grade fever. On physical examination, patient was drowsy. She was febrile, having temperature of 103^0F. Her blood pressure was 108/62 mm Hg, pulse rate was 118/minute, and respiratory rate was 18 breaths/minute and oxygen saturation was 98%. Systemic examination showed no abnormality. Patient was given injectable antipyretic and was then shifted to medicine ward for further management. She was admitted with PICC in situ. Prior to administration of antibiotics, peripheral venous blood and central catheter blood samples were collected separately and sent for cultures. Thereafter, intravenous ceftazidime was started. Blood samples were also sent for hematological and biochemical investigations. Total leucocyte count was 16800/mm^3 with 82% neutrophils and 18% lymphocytes. Hemoglobin was 11.5 gm/dl, platelet count was 98000 cells/mm^3 and erythrocyte sedimentation rate was 41mm/hour. C-reactive protein was 24.8 mg/dl. Procalcitonin level was 1.3 ng/ml. Renal function tests and liver function tests were within normal limits. Chest X-ray of the patient showed no abnormality. Ultrasound (whole abdomen) showed grade I fatty liver. Blood culture was done by an automated BACTEC System (BD) as per the manufacturer's instructions. After 14 hours of incubation, central catheter blood culture showed positive signal for microbial growth. The growth was then identified by the standard bacteriological techniques such as Gram staining, colony characteristics, motility and the biochemical tests.[16] Gram stained culture smear showed Gram negative bacilli with no specific arrangement. Subculture was done on blood agar and MacConkey's agar. After 24 hours of aerobic incubation at 37^0C, colonies on blood agar were circular, about 2-3 mm in diameter, greyish-white with smooth convex surface and entire edge (Figure-1), and MacConkey's agar showed lactose fermenting colonies (Figure-2). The isolate was motile, catalase positive and oxidase negative. It utilized glucose fermentatively on Hugh and Leifson's oxidation-fermentation media. It reduced nitrates to nitrites. It was indole positive, methyl red test positive, Voges-Proskauer test negative, citrate negative and urease negative. Arginine, lysine and ornithine decarboxylases tests were negative. On triple sugar iron agar, the isolate showed an acidic slant by an acidic butt reaction with abundant gas production without H_2S. The characteristics of our isolate were phenotypically and biochemially similar to *Escherichia coli* to some extent. Thus, the isolate was further identified by an automated VITEK 2 system (Biomerieux, France). Identification of the isolate was done by VITEK 2 GN card and antimicrobial susceptibility testing was performed using VITEK 2 AST-N 281card. The isolate was identified as *Leclercia adecarboxylata*. It was an extended spectrum beta-lactamase (ESBL) producer. The isolate was resistant to penicillins, all cephalosporins and monobactams. It was sensitive to combination of beta-lactam and beta-lactamase inhibitor antibiotics, cefoxitin and carbapenems. It was also susceptible to amikacin, gentamicin, colistin and tigecycline, but was resistant to ciprofloxacin and trimethoprim-sulfamethoxazole. The peripheral venous blood culture showed positive signal four hours later than the catheter blood culture. The peripheral venous blood culture also showed the growth of *Leclercia adecarboxylata* with similar antibiotic susceptibility pattern. These findings were indicative of catheter-related bloodstream infection (CRBSI). The treating clinician was informed about the blood culture and the antibiotic sensitivity report on the third day following sample submission. The patient's fever had not subsided by that time, and the laboratory tests revealed hyperleucocytosis at 18500/mm^3, thrombocytopenia at 87000 cells/mm^3 and C-reactive protein increased to 46.7 mg/dl. The treatment regimen was changed to intravenous meropenem and gentamicin, based on antibiotic susceptibility testing report. The PICC was removed. The catheter tip culture was also positive for *L. adecarboxylata* having same antibiogram. After 5 days of this targeted therapy, the patient became afebrile and well oriented. In addition, total leucocyte count dropped to 8670/mm^3 and C-reactive protein to 5.98 mg/dl. Follow up blood culture after 7 days of treatment was sterile. Patient was continued on meropenem and gentamicin for upto two weeks. The patient was discharged with the favourable clinical outcome.

III. Discussion:

Leclercia adecarboxylata has been acknowledged as an emerging pathogen in the recent years. The human gut is known to harbor this rare opportunistic Gram-negative bacillus.[3,5] It has been speculated that the infections caused by *L. adecarboxylata* are underestimated and have been under-reported for several decades, which is due to its sharing of several morphological and metabolic features with the sibling gut bacteria in the order Enterobacterales. This holds true in conjuction with *Escherichia coli*, as there is high degree of phenotypic overlap between *L. adecarboxylata* and *Escherichia coli*.[3,17,18] *L. adecarboxylata* has been recovered from various clinical samples such as blood, faeces, sputum, urine, wound pus and skin.[3,20,21] *L. adecarboxylata* is usually isolated as a part of polymicrobial cultures in immunocompetent indi viduals. Also, as stated by various authors, it might be the only isolate causing infections in immunocompromised patients.[2,6,22,23] It is also postulated that it is dependent on other bacteria to facilitate infection.[2,22] Exact knowledge of the route of transmission of *L. adecarboxylata* and the possible source of the infection is unclear.[13,23] Studies have shown that bacteremia due to *L. adecarboxylata* may be associated with destruction of the skin barrier, such as through trauma or burn wounds, alteration of normal microbial flora by antibiotic therapy, and peritoneal dialysis. The medical devices such as indwelling catheters also serves as important reservoirs for *L. adecarboxylata*.[6,11,19-21] Bacteremia caused by *L. adecarboxylata* is usually associated with immunosuppression and the presence of longstanding central venous lines, which

has been seen in our present case study also, where we have reported PICC-related bacteremia caused by extended-spectrum beta-lactamase-producing *L. adecarboxylata* in an immunocompromised patient with breast cancer. Our case findings are similar to the case reported in 2012 by Shin GW et al.[13] who had also documented catheter-related blood stream infection due to ESBL- producing multidrug-resistant *L. adecarboxylata* in a middle-aged female with right breast malignancy. The strain isolated by Shin GW et al.[13] showed resistance to β-lactams, aminoglycosides and sulfonamides, and harbored bla_{TEM-1} and bla_{CTX-M} group 1 and *intl1* genes (*dfrA12-orfF-aadA2*) as genetic determinants for resistance. However, in contrast to study done by Shin GW et al.[13], *L. adecarboxylata* isolated in our present case study was found to be susceptible to aminoglycosides but was resistant to ciprofloxacin. In 2020, Alosaimi R et al.[24] reported a case of catheter-related septicemia, in a 50-year-old female with an end-stage renal disease on hemodialysis, caused by ESBL producing *L. adecarboxylata*, who had responded well to meropenem and gentamicin. Similarly, our case also showed dramatic recovery with meropenem and gentamicin. Fernandez-Ruiz M et al.[25] documented the hemodialysis catheter-related *L. adecarboxylata* bacteremia in an elderly diabetic patient, diagnosed with renal cell adenocarcinoma. The organism isolated by Fernandez-Ruiz M et al.[25] was found to be sensitive to all antimicrobials with the exception of fosfomycin , and the case was successfully managed by catheter salvage (catheter was locked daily with ciprofloxacin at a concentration of 2 mg/ml added to sodium heparin 20 IU/ml), and by intravenous ceftriaxone given for 15 days. In 2013, De Mauri et al.[23] also reported a case of hemodialysis tunnelled central venous catheter infection due to *L. adecarboxylata*, susceptible to β-lactams, third-generation cephalosporins, quinolones, trimethoprim, aminoglycosides and carbapenems. De Mauri et al.[23] further stated that the patient was treated successfully with intravenous gentamicin and amoxicillin-clavulanic acid, in combination with locked-in therapy by gentamicin. In 2003, Mazzariol A et al.[12] reported an isolation of an SHV-12 ESBL-producing *L. adecarboxylata* strain from the bloodstream in a 58-year-old male with acute myeloid leukemia. Generally, *L. adecarboxylata* is considered a low-virulence pathogen with an excellent susceptibility profile, however emergence of multidrug resistant strains have been documented by various authors.[12-15,18,24] Of note, multidrug-resistant strains of *L. adecarboxylata* can become life threatening human pathogens by acquiring genetic determinants, including blaSHV, blaTEM-1, blaCTX-M group 1, and intl1 genes.[24] In our present case study, the strain which we have isolated is an ESBL producer, which has also been reported by various authors.[12,13,24] The expression of this resistance phenotype exhibited by our isolate could be due to acquiring resistance genes from other ESBL-producing bacteria. Thus, strict adherence to hand hygiene and adoption of aseptic clinical practices becomes crucial in averting the growing emergence of multidrug resistant bugs.

IV. Conclusions:

Our case highlights the emergence of *L. adecarboxylata* as a potential threat in patients with long standing intravenous catheters. We stress upon the importance of correct identification and antimicrobial susceptibility testing of this human pathogen. Prompt communication with the clinician and timely initiation of appropriate antibiotic treatment has proved to be the key for successful management of infection caused by this multi-drug resistant *L. adecarboxylata*. The opportunistic and nosocomial behaviour of this pathogen is associated with immunocompromised status and the implantation of intravenous catheters or other medical devices in debilitating patients. As the number of *L. adecarboxylata* infections continues to expand, further studies to understand the pathogenesis, risk factors and antibiotic resistance pattern of this Gram negative bacillus are required to be conducted.

Limitations:

Due to limited resources, molecular techniques for detection of extended-spectrum beta-lactamase-encoding genes could not be carried out.

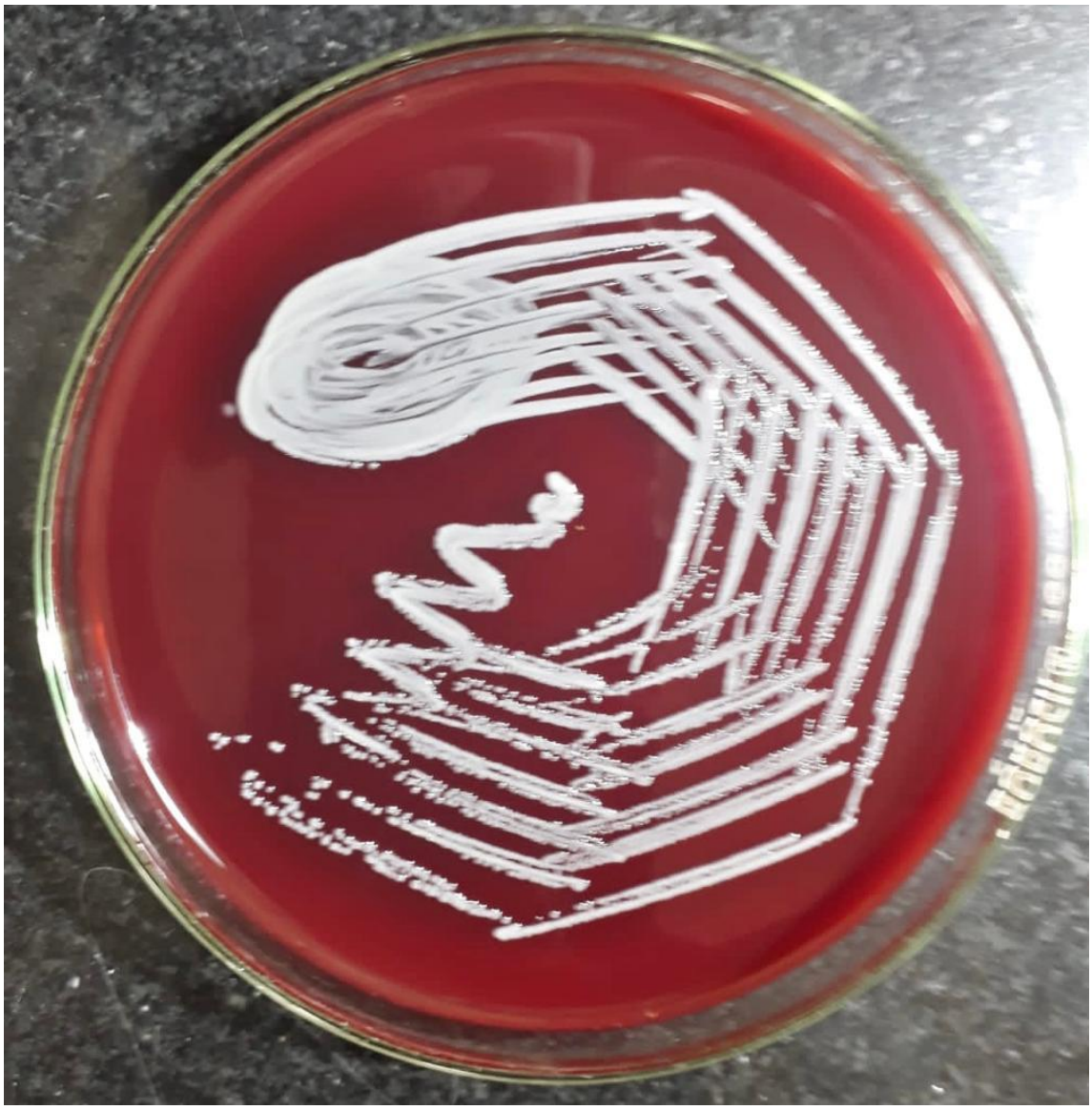

Figure-1: Grey-white colonies with smooth convex surface and entire edge on blood agar

Figure-2: Lactose fermenting colonies on MacConkey's agar

References:

[1]. Leclerc H. Biochemical study of pigmented Enterobacteriaceae. Ann Inst Pasteur. 1962; 102:726-741.
[2]. Anuradha M. Leclercia adecarboxylata isolation: case reports and review. J Clin Diagn Res. 2014; 8(12):3-4.
[3]. Stock I, Burak S, Wiedemann B. Natural antimicrobial susceptibility patterns and biochemical profiles of Leclercia adecarboxylata strains. Clin MicrobiolInfect Dis. 2004;10(8):724-33.
[4]. Tamura K, Sakazaki R, Kosako Y, Yoshizaki E. Leclercia adecarboxylata gen. nov., comb. nov., formerly known as Escherichia adecarboxylata. Current Microbiology. 1986;13(4):179-84.
[5]. Hess B, Burchett A, Huntington MK. Leclercia adecarboxylata in an immunocompetent patient. J Med Microbiol. 2008;57(7):896-98.
[6]. Spiegelhauer MR, Andersen PF, FrandsenTH, Nordestgaard RLM, Andersen LP. Leclercia adecarboxylata: a case report and literature review of 74 cases demonstrating its pathogenicity in immunocompromised patients. Infect. Dis. 2019;51(3):179-88.
[7]. Cicek M, Tuncer O, Bicakcigil A, Gursoy NC, Otlu B, Sancak B. A rarely isolated Gram-negative bacterium in microbiology laboratories: Leclercia adecarboxylata. Acta Microbiol Immunol Hung. 2018;65(2):241-44.
[8]. Fattal O, Deville JG. Leclercia adecarboxylata peritonitis in a child receiving chronic peritoneal dialysis. Pediatr. Nephrol. 2000;15:186-87.
[9]. Kim HM, Chon CY, Ahn SH, Jung SJ, Han KH, Moon BS et al. Fatal spontaneous bacterial peritonitis by Leclercia adecarboxylata in a patient with hepatocellular carcinoma. Int. J. Clin. Pract. 2008;62:1296-98.
[10]. Lee B, Sir JJ, Park SW, Kwak CH, Kim SM, Kim SB et al. A case of Leclercia adecarboxylata endocarditis in a woman with endometrial cancer. Am J Med Sci. 2009; 337(2):146-7.
[11]. Shah A, Nguyen J, Sullivan LM, Chikwava KR, Yan AC, Treat JR. Leclercia adecarboxylata cellulitis in a child with acute lymphoblastic leukemia. Pediatr. Dermatol. 2011;28(2):162-4.
[12]. Mazzariol A, Zuliani J, Fontana R, Cornaglia G. Isolation from blood cultureof a Leclercia adecarboxylata strain producing an SHV-12 extended-spectrum beta-lactamase. J. Clin. Microbiol. 2003;41(4):1738-39.
[13]. Shin GW, You MJ, Lee HS, Lee CS. Catheter-related bacteremia caused by multidrug-resistant Leclercia adecarboxylata in a

patient with breast cancer. J. Clin. Microbiol. 2012; 50(9):3129-32.
[14]. Papagiannitsis CC, Studentova V, Hrabak J, Kubele J, Jindrak V, Zemlickova H. Isolation from a nonclinical sample of Leclercia adecarboxylata producing a VIM-1metallo-β-lactamase. Antimicrob Agents Chemother. 2013;57(6):2896-7.
[15]. Riazzo C, Lopez-Cerero L, Rojo-Martin MD, Hoyos-Mallecot Y, Fernandez-Cuenca F, Martin-Ruiz JL et al. First report of NDM-1-producing clinical isolate of Leclercia adecarboxylata in Spain. Diagn. Microbiol. Infect. Dis. 2017;88:268-70.
[16]. Winn W, Allen S, Janda W, Koneman E, Procop G, Schreckenberger P et al.(eds.) Koneman's Color Atlas and Textbook of Diagnostic Microbiology. 6th edition. Philadelphia: Lippincott Williams &Wilkins;2006.
[17]. Nelson MU, Maksimova Y, Schulz V, Bizzarro MJ, Gallagher PG. Late-onset Leclercia adecarboxylata sepsis in a premature neonate. J Perinatol. 2013;33(9):740-2.
[18]. Makanera A, Conde M, Diallo MA, Conde M, Camara D, Diakite T et al. A multi-drug resistance pattern of a Leclercia adecarboxylata strain isolated from a urinary tract infection of a patient at China-Guinea friendship hospital of Kipe/Conakry. Int J Biol Chem Sci. 2018;12(4):1550-56.
[19]. Marina VP, Abidi S, Malhotra D. Leclercia adecarboxylata, an unusual hemodialysis catheter-related infection. Int. Urol. Nephrol. 2011;43:1257-58.
[20]. Dalamaga M, Pantelaki M, Karmaniolas K, Daskalopoulou K, Migdalis I. Isolation of Leclercia adecarboxylata from blood and burn wound after a hydrofluoric acid chemical injury. Burns. 2009;35(3):443-45.
[21]. Kashani A, Chitsazan M, Che K, Garrison RC. Leclercia adecarboxylata bacteremia in a patient with ulcerative colitis. Case Reports in Gastrointestinal Medicine. 2014; 1-4. doi: 10.1155/2014/457687.
[22]. Adapa S, Konala VM, Nawaz F, Javed T, Dhingra H, Gutierrez IA et al. Peritonitis from Leclercia adecarboxylata: An emerging pathogen. Clin Case Rep. 2019;7(4):829-31.
[23]. De Mauri A, Chiarinotti D, Andreoni S, Molinari GL, Conti N, De Leo M. Leclercia adecarboxylata and catheter- related bacteraemia: review of the literature and outcome with regard to catheters and patients. Journal of Medical Microbiology. 2013;62(10):1620-23.
[24]. Alosaimi R, Kaaki M. Catheter-related ESBL-producing Leclercia adecarboxylata septicemia in hemodialysis patient: An emerging pathogen? Case Reports in Infectios Diseases. 2020;1-3. https://doi.org/10.1155/2020/7403152
[25]. Fernandez-Ruiz M, Lopez-Medrano F, Garcia-Sanchez L, García-Reyne A, Ortuno de Solo T, Sanz-Sanz F, Aguado JM. Successful management of tunneled hemodialysis catheter-related bacteremia by Leclercia adecarboxylata without catheter removal: report of two cases. Int J Infect Dis. 2009;13(6):517-8.

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