ORIGINAL RESEARCH PAPER

Clinical Microbiology

CATHETER-RELATED BLOODSTREAM INFECTION CAUSED BY AN EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL) PRODUCING LECLERCIA ADECARBOXYLATA IN A HEMODIALYSIS PATIENT

KEY WORDS: Leclercia adecarboxylata, intravenous catheters, hemodialysis, CRBSI, ESBL, emerging pathogen

Vandana Sardana MD, Professor, Department of Microbiology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.

Sameer Rajeev Verma* MD, Professor, Department of Radiodiagnosis, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.*Corresponding Author

ABSTRACT

Leclercia adecarboxylata is being increasingly recognized as an opportunistic pathogen that causes wide range of infections, mainly in immunocompromised or debilitated patients. The medical devices such as indwelling intravenous catheters serves as important reservoirs for *L. adecarboxylata*, which can lead to bacteremia or sepsis. We report a case of catheter-related bloodstream infection caused by an extended-spectrum beta-lactamase (ESBL) producing *L. adecarboxylata*, in an elderly patient who was a known case of hypertension, diabetes mellitus type 2 and medical renal disease, and was on regular hemodialysis. Correct identification and timely initiation of an appropriate antimicrobial therapy resulted in the good clinical recovery of our patient.

Introduction:

Leclercia adecarboxylata is a motile, facultatively anaerobic, Gram-negative rod belonging to the family Enterobacteriaceae.[1] It was first identified by H. Leclerc in 1962. Formerly, it was designated as CDC Enteric group 41 and *Escherichia adecarboxylata*.[2,3] Based on protein electrophoretic and nucleic acid - based analyses, it was subsequently separated from the genus *Escherichia*, and was reclassified as *Leclercia adecarboxylata*.[3,4] It is ubiquitous in nature and also forms the part of the human gastrointestinal flora.[3,5]It has achieved a recognition as a pathogen of concern, both in immunocompetent as well as immunocompromised patients, with the potential to cause severe ailments such as bloodstream infection, pneumonia, urinary tract infection, wound infections, abscesses and diarrhea.[6,7] An opportunistic behaviour of *L. adecarboxylata*, causing infections in patients with impaired host defenses and debilitating illnesses such as those suffering from leukemia, cancer, hepatic cirrhosis and chronic kidney disease, has been documented by various authors. [8-11] Although, *L. adecarboxylata* is generally susceptible to most of the antibiotics in clinical use; however, drug resistant strains are not uncommon. *L. adecarboxylata* strains producing highly diversified enzymes such as extended-spectrum beta-lactamases and metallo-beta-lactamases have been reported.[12-15] We report a case of catheter-related bloodstream infection caused by an extended-spectrum beta-lactamase producing *L. adecarboxylata* in a hemodialysis patient with immunocompromised status.

Case Report

A sixty eight-year-old male presented in emergency unit with the chief complaint of high grade fever associated with chills and rigors since last 5 days. Patient also complained of cough with expectoration and difficulty in breathing for last 2 days. As per patient's medical records, he was a known hypertensive and diabetic for past 15 years. He had been diagnosed as a case of chronic kidney disease about nine months back, and had been undergoing hemodialysis. As stated in his records, the last dialysis was done 8 days back via a Permcath inserted in the right internal jugular vein, in another hospital. On clinical examination, patient was disoriented and had temperature of 102^{0}F. His blood pressure was 102/54 mm Hg, pulse rate was 116/minute, respiratory rate was 32 breaths/minute and oxygen saturation was 91%. On chest auscultation, bronchial breath sounds and crackles were heard in the right lung fields. Immediately, patient was shifted to intensive care unit and was put on ventilator support. He was admitted with Permcath in situ. Prior to the initiation of antibiotic therapy, peripheral venous blood and central venous catheter blood samples were collected and sent for cultures. Thereafter, intravenous cefotaxime was started. Arterial blood gas analysis revealed pH 7.329, pCO_2 35.7 mm Hg, pO_2 73.6 mm Hg. Total leucocyte count was 17400/mm^3 with 81% neutrophils, 16% lymphocytes and 3% eosinophils. Hemoglobin was 11.7 gm/dl, platelet count was 99000 cells/mm^3 and erythrocyte sedimentation rate was 46 mm/hour. C-reactive protein was 26.3 mg/dl. Procalcitonin level was 1.5 ng/ml. Renal function tests showed serum creatinine 2.3 mg/dl, blood urea 64 mg/dl, sodium 134 mEq/l, potassium 4.7 mmol/l, chloride 106 mmol/l and calcium 0.86 mg/dl. Random blood sugar was 318 mg/dl. Liver function tests were within normal limits. High resolution computed tomography (HRCT) scan of chest (Figure-1) showed bilateral pleural effusions and right lung upper lobar consolidation. Ultrasound abdomen (Figure-2) revealed bilateral raised renal cortical echogenicity with accentuated corticomedullary differentiation, suggestive of medical renal disease. Blood culture was done by an automated BACTEC System (BD) as per the manufacturer's instructions. After 12 hours of incubation, central venous catheter blood culture showed positive signal for microbial growth. Growth obtained was then identified by the standard bacteriological techniques such as Gram staining, colony characteristics, motility and biochemical tests.[1,16] Gram stained culture smear showed Gram negative bacilli with no specific arrangement. Subculture was done on sheep blood agar and MacConkey's agar. After 24 hours of aerobic incubation at 37^{0}C, colonies on blood agar were circular, 2-3 mm in diameter, grey-white with smooth convex surface and entire edge. MacConkey's agar showed lactose fermenting colonies. The isolate was catalase positive and oxidase negative. It utilized glucose fermentatively on Hugh and Leifson's oxidation-fermentation media. It reduced nitrate to nitrite. It was motile, indole test positive, methyl red test positive and Voges-Proskauer test negative. It was negative for citrate utilization, urea hydrolysis, arginine dihydrolase, lysine decarboxylase and ornithine decarboxylase tests. Triple sugar iron agar showed an acidic slant by an acidic butt reaction with abundant gas production without H_2S. The phenotypic and biochemical characteristics of our isolate were similar to *Escherichia coli* to much extent (Figure-3). An automated VITEK 2 system (Biomerieux) was then utilized for further confirmation of our isolate. Identification was done by VITEK 2 GN card and antimicrobial susceptibility testing by VITEK 2 AST-N 281 card. The isolate was identified as *Leclercia adecarboxylata*. It was an extended-spectrum beta-lactamase (ESBL) producer. The isolate was resistant to ampicillin, first-generation cephalosporins, second-generation cephalosporins, third-generation cephalosporins and aztreonam. It was sensitive to

cefoxitin, cefepime, amoxicillin-clavulanic acid, cefoperazone-sulbactam, piperacillin-tazobactam, meropenem, imipenem and ertapenem. It was also susceptible to gentamicin, amikacin, colistin, polymyxin B and tigecycline, but was resistant to ciprofloxacin, ofloxacin, levofloxacin and co-trimoxazole. The peripheral venous blood culture showed positive signal five hours later than the catheter venous blood culture. The peripheral venous blood culture also showed the growth of *L. adecarboxylata* with similar antibiotic susceptibility profile. These findings were suggestive of catheter-related bloodstream infection (CRBSI). The treating physician was informed about the blood culture report on the fourth day following sample submission. The patient's fever and respiratory distress had not subsided by that time, and the total leucocyte count got raised to 19300/mm^3, platelet count got dropped to 86000 cells/mm^3, and C-reactive protein increased to 52.4 mg/dl. On the basis of antibiotic susceptibility report, the treatment was changed to intravenous meropenem and gentamicin. The central venous catheter was also removed. The catheter tip culture also showed growth of *L. adecarboxylata* with identical antibiogram. After 4 days of this revised treatment, the patient became afebrile and his respiratory distress got settled. Total leucocyte count dropped to 8750/mm^3 and C-reactive protein to 6.14 mg/dl. Patient was extubated after one week of this treatment regimen. Follow up blood culture after 9 days of treatment was sterile. Patient was continued on meropenem and gentamicin for up to two weeks. The patient got discharged with the good clinical recovery.

Discussion:

In the recent years, *Leclercia adecarboxylata* has gained attention as an emerging pathogen of medical importance. *L. adecarboxylata* is usually misdiagnosed or unrecognized because of its phenotypic similarity to *Escherichia coli* and also due to the inability of automated systems to distinguish between *L. adecarboxylata* and *E. coli*.[3,17,18] Even though *L. adecarboxylata* exists widely in nature and has been recovered from water, food and other environmental sources,[3,5] its isolation from the various human samples such as blood, feces, urine, sputum and wound discharge has been also documented.[3,20,21] In immunocompetent patients, *L. adecarboxylata* usually forms a part of a mixed microbial growth.[2] Various authors have also stated that *L. adecarboxylata* might be the pure isolate causing infections in patients with impaired immunity.[2,6,22,23] As per various reports, bacteremia due to *L. adecarboxylata* can be linked to conditions associated with skin barrier dysfunction, including trauma, burn wounds, altered flora by prolonged antibiotic treatment and dialysis. Of note, longstanding intravenous catheter provides an important reservoir for *L. adecarboxylata*.[6,11,19-21] In our present case study, we have reported a hemodialysis catheter related bloodstream infection caused by an ESBL-producing *L. adecarboxylata* in an elderly patient with diabetes mellitus. Consistent to our case findings, Alosaimi R et al.[24], in 2020, had also reported a case of CRBSI, in a middle-aged patient with an end-stage renal disease on hemodialysis, caused by an ESBL producing *L. adecarboxylata*, who had responded well to meropenem and gentamicin. Similarly, our case also showed favorable clinical outcome with meropenem and gentamicin. In 2013, De Mauri et al.[23] documented a case of hemodialysis tunnelled central venous catheter infection due to *L. adecarboxylata*, sensitive to beta-lactams, third-generation cephalosporins, quinolones, trimethoprim, aminoglycosides and carbapenems. De Mauri et al.[23] further reported that the case was managed successfully with intravenous amoxicillin-clavulanic acid and gentamicin, and in combination with catheter locked-in therapy with gentamicin. Fernandez-Ruiz M et al.[25] had reported hemodialysis catheter-related *L. adecarboxylata* bacteremia in an elderly patient diagnosed with diabetes and renal cell adenocarcinoma. The isolate obtained by Fernandez-Ruiz M et al.[25] was found to be sensitive to all antibiotics with the exception of fosfomycin, and the case got treated well by intravenous ceftriaxone, and by catheter salvage (catheter locked with ciprofloxacin). In 2012, Shin GW et al.[13] had documented CRBSI due to ESBL-producing *L. adecarboxylata* in a middle-aged female with breast cancer. Shin GW et al.[13] observed that the isolate was resistant to beta-lactams, sulfonamides and aminoglycosides and harbored bla_{TEM-1} and bla_{CTX-M} group 1 and *intI1* genes (*dfrA12-orfF-aadA2*) as genetic determinants for drug resistance. Mazzariol A et al.[12] reported a case of BSI due to SHV-12 ESBL- producing *L. adecarboxylata*, in a patient with acute myeloid leukemia. In 2019, Gupta V et al.[26] from Haryana, reported a case of community-acquired pneumonia due to *L. adecarboxylata* in a previously healthy immunocompetent thirteen-month-old child. Gupta V et al.[26] stated that the blood culture was positive for growth of *L. adecarboxylata* which was detected by VITEK 2 and the isolate was found to be sensitive to all antibiotics tested. In 2015, Prakash MR et al.[27] had studied three case reports of nosocomial pneumonia caused by *L. adecarboxylata*, admitted to a neurosurgical centre in India, and it was found that the isolates of *L. adecarboxylata* obtained from all the three cases were susceptible to most of the antibiotics tested. However, in 2013, Eiland et al.[28] had reported a case of pneumonia due to multi-drug resistant *L. adecarboxylata* in a 55-year-old female with immunosuppressed status. Emergence of drug resistance in *L. adecarboxylata* poses a therapeutic threat, leaving behind limited treatment options.[12-15,18,24] In our case report, the antibiotic resistance profile displayed by *L. adecarboxylata* could be due to the drug resistance genes acquired from other bacteria. Inadequate hand hygiene often remains as a significant factor in the transmission of these drug resistant bugs. Continued vigilance for the development of drug resistance in *L. adecarboxylata* is crucial. Improving the abidance to standard precautions in health care may be adequate to scale down the burden of multi-drug resistant bugs in hospital settings.

Conclusions:

Our case study apprise the emergence of *L. adecarboxylata* as a nosocomial and opportunistic pathogen. Severe immunosuppresion and association with indwelling intravenous catheters appears to be the significant factors favouring *L. adecarboxylata* bacteremia. Correct identification and timely initiation of appropriate antibiotic therapy culminated in the dramatic clinical recovery of our patient. Burgeoning of drug resistance in *L. adecarboxylata* is an area of concern, emphasizing the need for aggressive infection prevention and control strategies.

Limitations:

Detection of ESBL encoding genes by molecular techniques could not be done due to resource constraints.

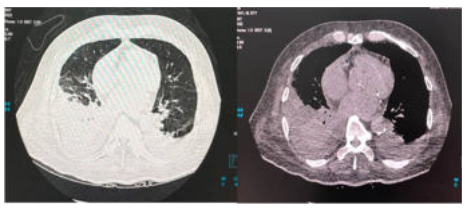

Figure-1: HRCT chest lung and soft tissue window images reveal bilateral pleural effusions and right lung upper lobar consolidation.

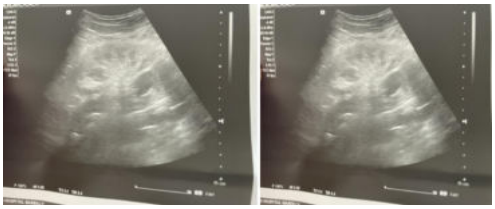

Figure-2: Ultrasound abdomen showing bilateral raised renal cortical echogenicity with accentuated corticomedullary differentiation, suggestive of medical renal disease.

Figure-3: Biochemical identification of Leclercia adecarboxylata 1&2- Hugh Leifson's O/F (glucose) test: fermentative; 3- Nitrate reduced to nitrite; 4- Triple sugar iron agar: A/A with gas; 5- Indole test positve; 6- Citrate not utilized; 7- Urea not hydrolysed; 8- Methyl red test positive; 9- Voges-Proskauer test negative; 10- Glucose fermented with acid and gas; 11- Lactose fermented; 12- Sucrose fermented; 13- Mannitol fermented; 14- Arginine dihydrolase test negative; 15- Lysine decarboxylase test negative; 16- Ornithine decarboxylase test negative

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