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Letter to the Editor

A Rare Case of Multidrug-resistant *Leclercia adecarboxylata* Catheter-related Bloodstream Infection and an Updated Brief Literature Review

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To the editor.

Antibiotic resistance is one of the most relevant problems in hospitals: the growth of resistant microorganisms in healthcare settings is a worrisome threat, raising the length of stay, morbidity, and mortality in patients infected with multidrug resistant bacteria.[1] Moreover, the steady progress in diagnostic techniques is rising concern about the emergence of new pathogens which were hardly known in the past years.

Leclercia adecarboxylata is a gram-negative, motile, facultative-anaerobic, oxidase-negative, mesophilic bacillus belonging to the *Enterobacteriaceae* family.[2] *L. adecarboxylata* was first described by H. Leclerc in 1962 and was previously known as Enteric group 410 or *Escherichia adecarboxylata*[3] since *Leclercia spp.* shares several structural and microbiological properties with the genus *Escherichia*. Due to those similarities, *L. adecarboxylata* infections might be more common than what is believed so far since past clinical cases might have been erroneously defined as *Escherichia* spp. infections. Moreover, most bacterial assays often could not distinguish these morphologically and metabolically similar bacteria.[4] Nevertheless, the availability of more sensitive testing methods (e.g., DNA hybridization, computer identification studies) like Matrix Assisted Laser Desorption/Ionization Time of Flight ("MALDI-TOF") mass spectrometry allowed a more precise species identification, eventually leading to the present categorization.[3] *L. adecarboxylata* can be found in various specimens and is involved in a wide range of clinical syndromes commonly related to immunocompromised hosts. Although most *Leclercia* spp isolates show high susceptibility to antibiotics, some multi-resistant strains have been reported in the literature. Here, we present a catheter related bloodstream infection caused by a multidrug resistant *L. adecarboxylata.*

Case Report. A 38-year-old transgender woman affected by gastric and duodenal diffuse large B-cell lymphoma in remission was admitted to our Infectious Diseases Department due to persistent and intense asthenia, weight loss, and recurring fever episodes. The last rituximab administration was performed 4 months before, and the antimicrobic prophylaxis was recently discontinued following bone marrow recovery. The patient assumed total parenteral nutrition through a tunneled central venous catheter (CVC) placed 5 months prior to the admission because of duodenal sub-stenosis subsequent to her hematologic condition. Moreover, she was affected by chronic hepatitis HBV-correlated, treated with tenofovir disoproxil fumarate, and several episodes of syphilis reinfection were recorded following her former sex worker activity. No HIV or HCV co-infections were detected. The chest CT scan performed in the Emergency Department showed a parenchymal and nodular thickening. Considering her risk factors for a healthcare-associated infection, piperacillin/tazobactam (4.5 g every 6 hours/day) was empirically started. At the admission, no catheter dysfunction and no signs of catheter-related infection were recorded, and neither an anti-methicillin-resistant *Staphylococcus aureus* (MRSA) nor an antimycotic agent was introduced.

A diagnostic bronchoscopy was also performed, but both microbiological tests (serology and cultures) and molecular biology assays performed on the bronchoalveolar lavage gave negative results. However, *L. adecarboxylata* was isolated from either peripheral and CVC blood culture performed at the hospital admission. Catheter-related bloodstream infection (CRBSI) was then diagnosed since a blood culture drawn from the line was positive 4 hours earlier than the

Table 1. Multidrug-resistant L. adecarboxylata antibiograms (S= susceptible, R= resistant).

	Catheter-drawn blood culture		***Peripheral blood culture***	
Microorganism	*Leclercia adecarboxylata*		*Leclercia adecarboxylata*	
Incubation period	5 hours		9 hours	
		MIC (mcg/ml)		MIC (mcg/ml)
Amikacin	S	2	S	2
Amoxicillin/clavulanic acid	R	>16	R	>16
Cefepime	S	≤0.12	S	≤0.12
Cefotaxime	S	≤0.25	S	≤0.25
Ceftazidime	S	≤0.12	S	≤0.12
Ceftazidime/avibactam	S	≤0.12	S	≤0.12
Ceftolozane/tazobactam	S	≤0.25	S	≤0.25
Ciprofloxacin	S	0.12	S	0.12
Colistin	S	≤0.5	S	≤0.5
Fosfomycin	R	>32	R	>32
Gentamicin	S	≤1	S	≤1
Imipenem	S	≤0.25	S	≤0.25
Meropenem	S	≤0.25	S	≤0.25
Piperacillin/tazobactam	S	≤4	S	≤1
Tobramycin	S	≤1	S	2
Trimethoprim/sulfamethoxazole	R	>160	R	>160

peripheral vein. This result was also consistent with the anamnestic data concerning suboptimal domiciliary management of the CVC, as she referred a sporadic nonsterile handling of the catheter entry site (for instance, contact with tap water). The antibiogram showed resistance to amoxicillin/clavulanate, fosfomycin, and trimethoprim-sulfamethoxazole (**Table 1**), so piperacillin/tazobactam (MIC ≤1) was maintained, and the catheter was promptly replaced with a peripherally inserted central catheter (PICC). A progressive clinical improvement was observed with a significant reduction in inflammatory markers. On day 14, the targeted systemic antibiotic therapy was discontinued. An esophagogastroduodenoscopy was later performed to assess the severity of the duodenal stenosis. A mass-forming inflammatory non-lymphomatous tissue was observed, and on day 21, a duodenal prosthesis was placed. In the following days, the patient was discharged with a semi-liquid diet and parenteral nutrition to recover a complete oral feeding.

Discussion and Literature Review. *Leclercia adecarboxylata* is a gram-negative bacillus member of the *Enterobacteriaceae* family with many structural and microbiological properties in common with the genus *Escherichia*.[2,3] The reclassification of this bacteria was achieved thanks to more sensitive testing methods such as DNA hybridization and computer identification studies.[2]

L. adecarboxylata has been recently recognized as an emerging pathogen[3,5] for which, thanks to the currently available diagnostic methods, it is possible to obtain an accurate identification.[3] Moreover, several analyses enlighten an ever-increasing number of multidrug-resistant strains[4,5,10] that should highlight the implications of this bacterial infection. *L. adecarboxylata* is a ubiquitous microorganism that may be found in aquatic environments and soil, as well as in the commensal gut flora of certain animals.[2] In our case, an exposition to an aquatic environment was identified (use of water to rinse the CVC), similar to a few cases reported in the literature.[6] Moreover, *L. adecarboxylata* might also be isolated from blood culture, skin wounds, peritoneal fluid, abscesses (e.g., peritonsillar and periovarian), feces, urine, and synovial fluid.[8] Several underlying conditions might favor *L. adecarboxylata* infections: for instance, wounds may act as a direct entry into the tissue, thus easing the pathogenicity, as well as catheters may be used as gateways in catheter-related bacteremia or peritonitis could be developed in patients undergoing dialysis or chemotherapy.[4]

The isolates more commonly mentioned in the literature show a high susceptibility to antibiotics.[4] They could be controlled with a variety of antibiotics, such as B-lactams, without witnessing therapeutic failures or needing second-line treatments.[10] Considering the EUCAST breakpoint for *Enterobacterales* and given the contemporary resistance to at least 1 antibiotic of 3 different classes showed in our *L. adecarboxylata* antibiogram, we consider peculiar our results since, to our best knowledge, only a few cases of resistant strains have been reported.[2] A more comprehensive evaluation

regarding natural antimicrobial susceptibility patterns was reported by Stock et al. from 94 *L. adecarboxylata* strains collected from several human specimens: the bacteria were naturally resistant to numerous antibiotic molecules, such oxacillin, clarithromycin, erythromycin, roxithromycin, ketolides, rifampin, glycopeptides, streptogramins, fusidic acid, lincosamides, penicillin G and fosfomycin but susceptible to most B-lactams, quinolones, aminoglycosides, tetracyclines, nitrofurantoine, folate pathway inhibitors, azithromycin and chloramphenicol. In addition, Extended-spectrum beta-lactamase (ESBL) and New Delhi metallo-beta-lactamase 1 (NDM)-producing *L. adecarboxylata* are also described. Three cases of ESBL producer isolates were reported: the first case was described from a patient with acute myeloid leukemia,[2] the second in a 47-year-old female with breast cancer,[10] and the third one in a 50-year-old female with end-stage renal disease.[5] Regarding NDM-producing *L. adecarboxylata*, two cases were reported: the first regarding a patient hospitalized for a foot trauma-related injury, and the second concerned an outbreak of 25 patients in intravenous total parental nutrition.[2]

L. adecarboxylata might cause monomicrobial infection in immunocompromised patients, while it is thought that this pathogen generally requires other coinfecting bacteria to establish infection in immunocompetent subjects.[4] However, some cases of monomicrobial infection were described in immunocompetent patients even without significant underlying comorbidities: only in one case the patient report a clinical history of chronic disease,[8] while in the other cases, no history indicative of a clinically compromised state was observed.[9] Prevalently, *L. adecarboxylata* infections are described in adults, but a wound infection and peritonitis were reported in two immunocompetent children.[2] *L. adecarboxylata* is implicated in several clinical syndromes, such as endocarditis,[2] bacteremia,[4,8] wound infection and cellulitis,[6] pharyngeal and peritonsillar abscesses,[9] urinary tract infections,[3] pneumonia[3] and peritonitis.[3] Most of these infections, as reported in our case, have been linked to immunosuppression and the simultaneous presence of central vascular catheter.[8] Additionally, as it appears from several reports, catheters could be considered important reservoirs for *L. adecarboxylata* bloodstream infection.[5,7,10] As a matter of fact, *L. adecarboxyalta* is not a fastidious pathogen: our strain grows both on blood and MacConkey agar.

Regarding treatment options, there are no shared guidelines or recommendations for *L. adecarboxylata* infections. Most isolates described are sensitive to tested antibiotics.[4] However, as described by Spiegelhauer et al., several strains of *L. adecarboxylata* displayed resistance to ampicillin (9/30 isolates resistant) and fosfomycin (8/10 isolates resistant), so these antibiotics should not be used as first-line for treatment. Stock et al. described the natural susceptibility patterns of *L. adecarboxylata*, showing that most isolated strains were sensible to B-lactams. Thus, *Leclercia* could be treated with this antibiotic class.[10] In our case, considering the multi-resistance pattern, we successfully treated our patient with the administration of piperacillin/ tazobactam.

Cosimo Colangelo[1], Giorgio Tiecco[1], Marco Di Gregorio[1], Susanna Capone[2], Roberto Luigi Allegri[2], Maria De Francesco[3], Francesca Caccuri[3], Arnaldo Caruso[3], Francesco Castelli[1] and Emanuele Focà[1].

[1] Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia-ASST Spedali Civili, Brescia, Italy.
[2] Unit of Infectious and Tropical Diseases, ASST Spedali Civili, Brescia, Italy.
[3] Section of Microbiology, Department of Molecular and Translational Medicine, University of Brescia-ASST Spedali Civili, P. Le Spedali Civili, 1, 25123, Brescia, Italy.

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Correspondence to: Emanuele Focà, Department Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, 25123 Brescia, Italy. Tel.: +39-0303995677. E-mail: emanuele.foca@unibs.it

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