Ann Acad Med Singap 2021;50:643-5
https://doi.org/10.47102/annals-acadmedsg.202195

Leclercia adecarboxylata bacteraemia: Clinical features and antibiotic susceptibilities in 2 hospitals in Singapore

Dear Editor,

Leclercia adecarboxylata was first described by Leclerc in 1962.[1] Formerly designated as enteric group 41 and previously known as *Escherichia adecarboxylata*, it is a motile, gram-negative bacillus in the family *Enterobacteriaceae*.[2] It can be found in various environmental sources, as well as the gastrointestinal tract of humans and animals.[2,3] Following improved diagnostic techniques, *L. adecarboxylata* is increasingly recognised as a pathogen of clinical significance. It has been isolated from wounds, abdominal fluid and blood.[4] It is usually encountered as a monomicrobial infection in immunocompromised individuals or as part of a polymicrobial infection in immunocompetent hosts.[5] While previously reported isolates were susceptible to most antibiotics,[5,6] drug-resistant strains including extended-spectrum beta-lactamase (ESBL)-producing[7] and carbapenemase-producing strains[8-10] are increasingly reported.

Our review of microbiology laboratory records from 1 January 2005 to 31 May 2021 identified 8 cases of *L. adecarboxylata* bacteraemia in Singapore General Hospital and Changi General Hospital, Singapore. We present the antibiotic susceptibility profiles of all 8 isolates that were collected as part of laboratory surveillance. We also present the clinical features of 6 patients with *L. adecarboxylata* bacteraemia. Patient consent for review of 6 patients' medical records was waived by the SingHealth Centralised Institutional Review Board (Ref: 2020/2861). The medical records of the other 2 patients who presented after 1 November 2017 were not accessed, in compliance with the Human Biomedical Research Regulations 2017.

Over a period of 13 years from January 2005 to October 2017, a total of 6 patients were diagnosed with *L. adecarboxylata* bacteraemia. The mean age of the patients was 66 years old (range 49–79). All were Chinese males. Diabetes mellitus (100%) and hypertension (83.3%) were the most common comorbidities. Five out of 6 patients (83.3%) presented with primary bacteraemia where the source of infection was unknown. A skin and soft tissue infection was thought to be the source of infection in the other 1 patient. *L. adecarboxylata* was part of a polymicrobial bacteraemia in 3 patients. The most common co-infecting organism was *Klebsiella pneumoniae* (2 out of 3 patients). *Enterobacter cloacae* complex, *Acinetobacter lwoffii, Pantoea* spp., methicillin-susceptible *Staphylococcus aureus* and *Bacillus* spp. were the other co-infecting organisms. Bacteraemia, including the co-infecting organisms, cleared quickly once appropriate antibiotic therapy was initiated—there was no persistent bacteraemia in all 5 patients who had blood cultures repeated.

During the evaluation for the source of bacteraemia, advanced malignancies, namely metastatic lung malignancy and advanced hepatocellular carcinoma (HCC) with tumour thrombus in the portal vein, were incidentally diagnosed in 2 patients. The malignancies may have led to disruption in the mucosal barrier, leading to translocation of intraluminal bacterial flora across the damaged mucosa into the blood stream. This may explain why co-infecting organisms are commonly *Enterobacteriaceae* in polymicrobial bacteraemia involving *L. adecarboxylata*. In patients with *L. adecarboxylata* bacteraemia without an evident source, we recommend that patients undergo evaluation to identify the source of bacteraemia. An occult malignancy should be considered, especially if clinical clues such as weight loss or unexplained anaemia are present.

The isolates of *L. adecarboxylata* were susceptible to most of the tested antibiotics (Table 1). Detected in vitro antibiotic resistances were infrequent, and limited to first-generation cephalosporin (cephalothin and cefazolin) and trimethoprim/sulfamethoxazole. An intravenous beta-lactam or ciprofloxacin was the most commonly used empirical antibiotic. After antibiotic susceptibility was known, most patients were switched to oral ciprofloxacin. Two patients passed away within 30 days from the date of diagnosis for *L. adecarboxylata* bacteraemia. The first patient presented with sepsis, and was found to have advanced HCC. Death occurred 11 days after the diagnosis of bacteraemia. The other patient clinically recovered during the hospital stay, and was discharged to complete a 2-week course of ciprofloxacin. He passed away 3 weeks after discharge in a different institution.

While previously described isolates showed susceptibility to most antibiotics,[5,6] multidrug-resistant strains have been increasingly reported.[7,8,10] Among the

Table 1. Antibiotic susceptibility test results for the 8 *L. adecarboxylata* isolates

Antibiotics tested	Susceptible isolates (%)
Penicillins	
Ampicillin	8/8 (100)
Ampicillin/sulbactam	5/5 (100)
Amoxicillin/clavulanic acid	8/8 (100)
Piperacillin/tazobactam	8/8 (100)
Cephalosporins	
Cephalothin	0/1 (0)
Cefazolin	2/7 (28.5)
Ceftriaxone	8/8 (100)
Cefotaxime	4/4 (100)
Ceftazidime	5/5 (100)
Cefepime	8/8 (100)
Monobactams	
Aztreonam	8/8 (100)
Carbapenems	
Imipenem	8/8 (100)
Meropenem	6/6 (100)
Ertapenem	8/8 (100)
Aminoglycosides	
Amikacin	8/8 (100)
Gentamicin	8/8 (100)
Tobramycin	1/1 (100)
Fluoroquinolones	
Ciprofloxacin	8/8 (100)
Levofloxacin	6/6 (100)
Folate synthesis inhibitors	
Trimethoprim/sulfamethoxazole	5/6 (83.3)
Tetracyclines	
Minocycline	1/1 (100)
Nitrofurans	
Nitrofurantoin	5/5 (100)

Not all isolates were tested for all drugs listed. Minimum inhibitory concentration values are not available as disk diffusion testing was employed for susceptibility testing.

8 isolates that we have identified in the 2 hospitals in Singapore from 2005 to 2021, multidrug resistance was not an issue. When treating a patient with community-acquired *L. adecarboxylata* bacteraemia in which antibiotic susceptibility is still unavailable, we suggest an empirical regime consisting of an intravenous third-generation cephalosporin (e.g. ceftriaxone) until a polymicrobial source of infection, such as perforated viscus, is excluded. Alternatively, if there is no undrained collection that may raise concern for treatment-emergent resistance, ciprofloxacin may be considered. Intravenous ampicillin may also be used if there is no suspicion of co-infection by other bacteria. However, when there is poor clinical response to an empirical first-line antibiotic, antibiotic treatment should be broadened because of the possibility of a polymicrobial bacteraemia, and the increasing prevalence of multidrug-resistant *L. adecarboxylata* isolates.[7-9] Among our patients, it is noteworthy that co-infecting organisms include *E. cloacae* complex and *A. lwoffii*—organisms that have intrinsic or developed resistance to third-generation cephalosporins.

A limitation of our study is the absence of more recent isolates—while the review of laboratory records extended to 31 May 2021, the last isolate identified was in August 2018. Ongoing surveillance is necessary to identify the emergence of multidrug-resistant *L. adecarboxylata* in Singapore.

When treating patients with *L. adecarboxylata* bacteraemia, clinicians should be aware of the possibility of a polymicrobial bacteraemia, and the emergence of multidrug-resistant strains worldwide. Our study shows that drug resistance is not yet a common issue in Singapore. Further studies, involving other Singapore and overseas hospitals, are needed to better elucidate the antibiotic susceptibilities of this organism. In cases where the source of infection is not evident, an occult malignancy should be considered, especially if clinical clues are present.

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