Polymyxin-Resistant Clinical Isolates of *Escherichia coli*

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A surveillance study to identify patients from the community with *Escherichia coli* resistant to broad-spectrum cephalosporins discovered two isolates that were also resistant to polymyxin B and colistin. One isolate from a patient in the community and a second from a patient who received multiple courses of polymyxin B also possessed a CTX-M-15 enzyme. Resistance to cationic peptides in *E. coli* is unusual, and testing for susceptibility to these agents should be performed.

Clinical infections due to multidrug-resistant, extremely drug-resistant, and panresistant strains of Gram-negative bacteria have been steadily increasing over the past decade (1, 2, 6, 13, 14). While strains resistant to polymyxin B and colistin have been identified rarely (7, 15), we report here two cases in which polymyxin B- and colistin-resistant *E. coli* isolates were identified. One was from a surveillance study of 90 *E. coli* single-patient isolates resistant to broad-spectrum cephalosporins that was conducted from March 2009 through September 2009, and the second isolate was identified in May 2010.

The first strain was isolated from an 83-year-old female living at home with a past medical history of hypertension and hyperlipidemia and a remote history of a brain mass that required a resection and radiation therapy. She presented to the emergency department with fever, chills, nausea, bilateral lower extremity erythema, and a white blood cell (WBC) count of 13,000 and was admitted with a diagnosis of cellulitis. Blood cultures and urinalysis were performed. The patient was treated with vancomycin and piperacillin-tazobactam, followed by vancomycin and ampicillin-sulbactam. Urinalysis revealed positive leukocyte esterase with 10 to 20 WBCs per high-power field. Urine cultures yielded 50,000 colonies of *E. coli* which were identified and for which MICs were determined by the clinical microbiology laboratory using BD Phoenix NMIC/ID-123 panels (Becton, Dickinson and Company, Sparks, MD). Isolates were resistant to ceftriaxone (MIC, 8 μg/ml), levofloxacin (MIC, >4 μg/ml), and trimethoprim-sulfamethoxazole (MIC, >2/38 μg/ml) and susceptible to meropenem (MIC, ≤1 μg/ml). Isolates were resistant to polymyxin B and colistin by broth microdilution according to CLSI guidelines (5) and Etest methodology performed according to the manufacturer’s specifications (bioMérieux North America) (Table 1). A renal sonogram showed no hydronephrosis, but the patient did have a distended bladder and was unable to void at the time of sonogram. The patient was treated with 50 mg of nitrofurantoin every 8 h for 7 days. In addition, the isolate harbored a CTX-M-15 extended-spectrum-β-lactamase when analyzed by PCR as previously described (13). Review of the patient’s past medical history revealed no identifiable risk factors, including recent hospital admission and recent antibiotic use, for the isolation of polymyxin B-resistant *E. coli*.

The second patient was a 56-year-old male nursing home resident. His past medical history included multiple sclerosis, pulmonary embolism, seizure disorder, tracheostomy for respiratory failure, gastrostomy secondary to dysphagia, congestive heart failure, diabetes mellitus, and peripheral inserted central catheter line placements with multiple hospital admissions. From May 2009 through May 2010, the patient was treated for pneumonia on eight different occasions with polymyxin B and meropenem for sputum cultures yielding *Acinetobacter baumannii*, *Providencia* species, *E. coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. On two additional instances, he also received polymyxin B and tigecycline for *K. pneumoniae* bacteremia. On 5 of the 10 courses of treatment with polymyxin B regimens, the patient, with normal serum creatinine, was treated with 500,000 U of polymyxin B daily for his Gram-negative infections, which may have led to the selection of polymyxin B-resistant isolates.

The *E. coli* isolate was resistant to polymyxin B and colistin (Table 1), as well as levofloxacin (MIC, >4 μg/ml), trimethoprim-sulfamethoxazole (MIC, >2/38 μg/ml), and ceftriaxone (MIC, >32 μg/ml). CTX-M enzymes were not detected by PCR in this isolate. Although we have not investigated the mechanism(s) of resistance to polymyxin in these isolates, numerous mechanisms, including alterations in lipid A, alterations of net surface charge, outer membrane protein changes, efflux mechanisms, and production of proteolytic enzymes, have been reported (4). Modification of lipid A with 4-amino-4-deoxy-t-arabinose, which is controlled by the PmrA/PmrB regulatory system, has been documented in polymyxin-resistant mutants of *E. coli* (3). However, the isolation of polymyxin-resistant strains of *E. coli* is worrisome because of the omnipresence of *E. coli* strains, especially in the urinary tract. The possibility that polymyxin-resistant, community-acquired strains exist increases the dilemma of treating patients with infections caused by such organisms. With the increasing isolation of virulent strains of *E. coli* resistant to broad-spectrum cephalosporins due to CTX-M and/or *K. pneumoniae* carba-

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penemase β-lactamases and additional co-resistance to many other classes of antibacterial agents (8, 9, 13, 14), cationic peptides, including polymyxin B and colistin, will increasingly be required for therapy. Further selection of resistance to cationic peptides may be expected, as was reported for K. pneumoniae and Enterobacter aerogenes (1, 12). Clinical microbiology laboratories should consider testing for polymyxin and colistin susceptibility, and E. coli can now be added to the ESKAPE acronym for multiresistant clinical infections (Enterococcus, Staphylococcus aureus, Klebsiella, Acinetobacter, Pseudomonas, Enterobacter, and E. coli) (2, 10, 11).

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We have no conflicts of interest.

REFERENCES


### TABLE 1. MICs determined by Etest and broth microdilution

<table>
<thead>
<tr>
<th>E. coli isolate or strain</th>
<th>Polymyxin B</th>
<th>Colistin (polymyxin E)</th>
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<tbody>
<tr>
<td></td>
<td>Etest</td>
<td>Microdilution</td>
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<tr>
<td></td>
<td>MIC</td>
<td>MBC a</td>
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<tr>
<td>ATCC 25922</td>
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</tr>
<tr>
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<td>16</td>
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<tr>
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</tbody>
</table>

a Values are in micrograms per milliliter.

b MBC, minimal bactericidal concentration.