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# *Klebsiella pneumoniae* ST147 Coproducing NDM-7 Carbapenemase and RmtF 16S rRNA Methyltransferase in Minnesota

**Chang-Seop Lee,[a,b] Shawn Vasoo,[c] Fupin Hu,[a,d,e] Robin Patel,[c] Yohei Doi[a]**

Division of Infectious Diseases, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA[a]; Department of Internal Medicine and Research Institute of Clinical Medicine, Chonbuk National University Medical School and Hospital, Jeonju, Republic of Korea[b]; Division of Clinical Microbiology, Department of Laboratory Medicine and Pathology and Division of Infectious Diseases, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA[c]; Institute of Antibiotics, Huashan Hospital, Fudan University, Shanghai, China[d]; Key Laboratory of Clinical Pharmacology of Antibiotics, Ministry of Health, Shanghai, China[e]

Acquired 16S rRNA methyltransferase (16S-RMTase) has emerged as a mechanism of high-level aminoglycoside resistance among Gram-negative pathogens worldwide (1). RmtF is a 16S RMTase which was identified in a single *Klebsiella pneumoniae* isolate on La Réunion Island in 2011 (2). The isolate also produced NDM-1 and was resistant to all β-lactams and aminoglycosides tested. Subsequently, *rmtF* was identified in 34 of 140 aminoglycoside-resistant *Enterobacteriaceae* isolates collected in India (3). Twenty of these 34 isolates also carried $bla_{NDM-1}$. Here, we report the identification of a *K. pneumoniae* strain coproducing NDM-7 and RmtF and an *Escherichia coli* strain producing NDM-7 from a patient who was admitted to a hospital in Minnesota.

In 2012, *K. pneumoniae* was isolated from the intra-abdominal abscess of a 69-year-old man who had been referred from India to a tertiary hospital in Minnesota. He had presented with abdominal pain and jaundice and had undergone endoscopic retrograde pancreatic cholangiography with biliary stenting twice while in India. In Minnesota, he underwent laparoscopic pancreaticoduodenectomy, and a diagnosis of adenocarcinoma of the pancreatic head was made. Six days postoperatively, he developed a complicated intra-abdominal infection for which he underwent percutaneous drainage of a fluid collection. The culture grew an *E. coli* isolate (EC1) that was resistant to ceftriaxone and susceptible to carbapenems. One week into treatment with piperacillin-tazobactam, another drain was put in place, and a repeat culture grew carbapenem-resistant *K. pneumoniae* (KP1). Six weeks later, the drains were adjusted, and repeat cultures grew carbapenem-resistant *K. pneumoniae* (KP2) and carbapenem-resistant *E. coli* (EC2). He initially received colistin, vancomycin, metronidazole, and caspofungin after KP1 was isolated, but treatment was limited by renal toxicity; therapy was completed with vancomycin, tigecycline, meropenem, and caspofungin. He ultimately made a complete recovery, and the abdominal drains were removed.

KP2 and EC2 were available for further analysis; they were resistant to all β-lactams tested, including carbapenems tested by broth microdilution (Sensititre GNX2F; Trek Diagnostics, Oak-

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Address correspondence to Yohei Doi, yod4@pitt.edu.

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**TABLE 1** MICs of *K. pneumoniae* and *E. coli* isolates, their transformants, and control strains

| Drug | MIC (μg/ml) | | | | | | |
|---|---|---|---|---|---|---|---|
| | *K. pneumoniae* KP2 | *E. coli* TOP10 transformants for KP2 | | | *E. coli* EC2 | *E. coli* TOP10 transformant for EC2 (pNDM-7-EC2) | *E. coli* TOP10 |
| | | pCTX-M-15 | pNDM-7-KP2 | pRmtF | | | |
| Imipenem | >8 | ≤1 | 2 | ≤1 | >8 | 2 | ≤1 |
| Ertapenem | >4 | ≤0.25 | 4 | ≤0.25 | 4 | 4 | ≤0.25 |
| Doripenem | >2 | ≤0.12 | >2 | ≤0.12 | >2 | >2 | ≤0.12 |
| Meropenem | >8 | ≤1 | 4 | ≤1 | 2 | 4 | ≤1 |
| Ceftazidime | >16 | >16 | >16 | ≤1 | >16 | >16 | ≤1 |
| Cefotaxime | >32 | >32 | >32 | ≤1 | >32 | >32 | ≤1 |
| Ticarcillin-clavulanate | >128/2 | 128/2 | >128/2 | ≤16/2 | >128/2 | >128/2 | ≤16/2 |
| Piperacillin-tazobactam | >64/4 | ≤8/4 | >64/4 | ≤8/4 | >64/4 | >64/4 | ≤8/4 |
| Cefepime | >16 | >16 | 16 | ≤2 | >16 | 16 | ≤2 |
| Aztreonam | >16 | >16 | ≤2 | ≤2 | 16 | ≤2 | ≤2 |
| Gentamicin | >8 | ≤1 | ≤1 | >8 | >8 | ≤1 | ≤1 |
| Tobramycin | >8 | ≤1 | ≤1 | >8 | 8 | ≤1 | ≤1 |
| Amikacin | >32 | 8 | ≤4 | >32 | ≤4 | ≤4 | ≤4 |
| Ciprofloxacin | >2 | ≤0.25 | ≤0.25 | ≤0.25 | >2 | ≤0.25 | ≤0.25 |
| Levofloxacin | 8 | ≤1 | ≤1 | ≤1 | >8 | ≤1 | ≤1 |
| Doxycycline | 8 | ≤2 | ≤2 | ≤2 | >8 | ≤2 | ≤2 |
| Minocycline | 16 | ≤2 | ≤2 | ≤2 | 8 | ≤2 | ≤2 |
| Tigecycline | 1 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 |
| Trimethoprim-sulfamethoxazole | >4/76 | >4/76 | ≤/0.5/9.5 | ≤0.5/9.5 | >4/76 | ≤0.5/9.5 | ≤0.5/9.5 |
| Colistin | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 |
| Polymyxin B | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 | ≤0.25 |

wood Village, OH) and interpreted by Clinical and Laboratory Standards Institute guidelines (Table 1) (4). KP2 was additionally resistant to all aminoglycosides tested. The sequence types (STs) of KP2 and EC2 were ST147 and ST617, respectively (5, 6). Both isolates were positive for $bla_{\text{NDM-7}}$ and $bla_{\text{CTX-M-15}}$ by PCR and sequencing of the entire genes (7). NDM-7 is a variant of NDM-1 with a two-amino-acid substitution that appears to have improved hydrolytic efficiency of carbapenems compared with NDM-1 (8). KP2 was also positive for *rmtF* by PCR and sequencing of an internal fragment of the gene. The plasmids of KP2 and EC2 were extracted by the standard alkaline lysis method and used to transform competent *E. coli* TOP10 cells to obtain transformants harboring plasmids with these genes using lysogenic agar plates containing ampicillin or gentamicin (9). As a result, KP2 yielded three different transformants demonstrating resistance to cephalosporins, carbapenems, and aminoglycosides, each with $bla_{\text{CTX-M-15}}$, $bla_{\text{NDM-7}}$, or *rmtF*, whereas EC2 yielded a transformant with $bla_{\text{NDM-7}}$ (Table 1). The replicon could be determined only for the $bla_{\text{CTX-M-15}}$-carrying plasmid of KP2, which was assigned to IncR (10). Nonetheless, the identification of $bla_{\text{NDM-7}}$, a relatively infrequent $bla_{\text{NDM}}$ allele (11), in both KP2 and EC2 suggested that the $bla_{\text{NDM-7}}$-carrying plasmids in these two strains may share an origin. The emergence of *K. pneumoniae* coproducing NDM metallo-β-lactamase and RmtF 16S-RMTase in the United States highlights the continuous threat of global dissemination of highly resistant enteric organisms by means of travel.

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