First Case of New Delhi Metallo-β-Lactamase 1–Producing Escherichia coli Infection in Japan

To the Editor—Emergence of multidrug-resistant organisms is a threat to public health, because there is limited effort devoted to the development of new antibiotics [1]. Multiple new mechanisms of resistance have been described recently, including a new type of carbapenem resistance gene, blaNDM−1, reported in 2009 [2]. Infections due to strains with blaNDM−1 have been reported in India, Pakistan, the United Kingdom, and the United States [2–4].

We report the first case, to our knowledge, of New Delhi metallo-β-lactamase 1 (NDM-1)–producing Escherichia coli infection in Japan. A 54-year-old Japanese man traveled to India for business in March 2009. During his trip, he developed dysarthria, blurring of his left eye, and tingling in his right upper extremity. He was admitted to a local hospital in India on 25 March 2009 with a diagnosis of Guillian–Barre syndrome, and he subsequently developed bradycardia, hypotension, and respiratory failure. He was intubated and received mechanical ventilation. Once he was deemed stable enough to travel with mechanical ventilation, he was transferred to the intensive care unit at Dokkyo Medical University Hospital in Japan on 4 April 2009. One month after the transfer, the patient developed fever, and 2 sets of blood cultures showed 2 types of E. coli simultaneously. One isolate was an extended-spectrum β-lactamase (ESBL)
producer (meropenem minimum inhibitory concentration [MIC], $\leq 1 \mu g/mL$), and the other isolate was a pan-resistant organism except for minocycline (meropenem MIC, $>8 \mu g/mL$). ESBL-producing E. coli was isolated from urine and sputum specimens. No enhancement was observed when the ceftazidime disk was used in the sodium mercaptoacetic acid screening test for the second pan-resistant isolate. When the imipenem disk was used, it was equivocal, with a zone enhancement of 4 mm. Although in vitro testing showed resistance to fourth-generation cephalosporins for both isolates, the patient was treated with ceftazidime-sulbactam, and his bacteremia cleared. He was transferred to a rehabilitation facility 5 months later, and there was no subsequent isolation of the panresistant E. coli strain.

At the time, we performed molecular testing for known metallo-$\beta$-lactamases, including blaIMP and blaVIM genes, using polymerase chain reaction (PCR), but all tests had negative results. The presence of class 1 integron aminoglycoside acetyltransferase-6' type 1b (aacA7) was confirmed by PCR [5]. After new metallo-$\beta$-lactamases were reported in patients who received care in India and Pakistan, we retrieved the E. coli isolates from storage and restested them for NDM-1 using specific primers targeting the gene. The result was consistent with NDM-1 (Figure 1). When comparing the DNA sequence of the PCR product using the Basic Local Alignment Search Tool, the isolates matched 100% (457 of 457 base-pairs) with NDM-1 (GenBank accession number: FN396876.1).

In conclusion, this was, to our knowledge, the first reported case of infection due to NDM-1–producing E. coli (NDM-1 Dok01) in Japan. The sodium mercaptoacetic acid test showed a larger enhancement of the zone of inhibition with imipenem. We recommend molecular testing for NDM-1 of Enterobacteriaceae isolates when there is carbapenem resistance according to conventional testing, especially in patients with exposure to health care in South Asia.

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Shingo Chihara,1,2 Katsuko Okuzumi,2 Yoshitaka Yamamoto,1 Shinji Oikawa,1 and Akira Hishinuma1,2

1Department of Clinical Laboratory Medicine, 2Division of Infection Control, Dokkyo Medical University, Mibu, Tochigi, Japan

**References**


Correspondence: Dr Akira Hishinuma, Dept of Clinical Laboratory Medicine, Dokkyo Medical University, and Div of Infection Control, Dokkyo Medical University Hospital, 880 Kitakobayashi, Mibu, Shimotsuga, Tochigi, 321-0293 Japan (a-hishi@dokkyomed.ac.jp).

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