Short Communication

Isolation of OXA-48 Carbapenemase-Producing Klebsiella pneumoniae ST101 from an Overseas Traveler Returning to Japan

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SUMMARY: OXA-48 carbapenemase-producing organisms have emerged rapidly worldwide and may be transmitted through patients who receive medical care abroad. To our knowledge, this is the second case of OXA-48-producing Klebsiella pneumoniae isolated from a patient who had returned to Japan after receiving treatment abroad.

Infections by multiderug-resistant gram-negative rods present a great public health concern and have continued to spread worldwide (1). Receiving medical care abroad has been suggested as a potential route of transmission of multidrug-resistant organisms (MDROs) (2). β-Lactamase genes, particularly those coding for carbapenemase, have a high transmissibility rate and play a significant role in the development of multiderug resistance. The OXA-48 carbapenemase was first isolated from Enterobacteriaceae in Istanbul, Turkey in 2001 (3). Since then, outbreaks with enormous clinical impact have been reported worldwide (4–7). Furthermore, the isolation of OXA-48-producing organisms from patients transferred from foreign countries to their native countries has also been increasingly reported (8,9). The first case of OXA-48 carbapenemase-producing Klebsiella pneumoniae and Escherichia coli was reported in Japan in December 2012 (9). Here we report the second case of an OXA-48-producing K. pneumoniae isolate from a clinical sample obtained from a patient returning to Japan.

An 84-year-old Japanese man with no significant past medical history or exposure to antimicrobial agents went on a 15-day tour to Egypt and Turkey in April 2012. On the 14th day of his trip, he presented at a hospital in Cairo, Egypt with vomiting, diarrhea, fever, and jaundice. He was subsequently diagnosed with traveler’s diarrhea, septic shock, and obstructive jaundice and admitted to the intensive care unit (ICU), where administration of meropenem, ciprofloxacin, and metronidazole was initiated. Isolation of OXA-48-producing organisms from the patient was considered to be at risk of infection by antimicrobial-resistant organisms. Therefore, he was kept in a single room with contact precaution. Screening results of a stool culture to identify MDROs were positive for K. pneumoniae, which was thought to be resistant to third and fourth generation cephalosporins and levofloxacin. The minimum inhibitory concentration (MIC) of imipenem was 4 mg/L as measured using the MicroScan WalkAway™ system (Siemens AG, Munch, Germany). The MIC was also determined using the manual broth microdilution method as per the Clinical and Laboratory Standards Institute (CLSI) criteria (Table 1) (10). Polymerase chain reaction (PCR) with specific primers was used to detect genes encoding plasmid-mediated AmpC β-lactamases (blaACC, blaCIT, bladHA, bladBC, blaOXA, and blamOX), metallo-β-lactamases (blaAMH, blabIM, blamDM, blamIP, blamNDM, blasIM, and blasSPK) (11), carbapenemases (blaqBIC, blaqPC, blaqOXA10, blaqOXA23, blaqOXA24, blaqOXA48, and blaqOXA51) (2,12), and extended-spectrum β-lactamases (ESBL) (blaqCTX-M, blaqPER, blaqSHV, and blasEM) (12,13). DNA sequences of open reading frames of the drug-resistant PCR-positive genes were determined. The multidrug-resistant K. pneumoniae isolate harbored 3 ESBL-encoding genes (blaqTEM, blasSHV, and blasCTX-M-14) and a carbapenemase-encoding gene (blaqOXA48), but no genes encoding plasmid-mediated AmpC β-lactamases or metallo-β-lactamase. Multilocus sequence typing (MLST) was performed as described in the K. pneumoniae MLST Database (http://www.pasteur.fr/recherche/genopole/PF8/mlst/Kpneumoniae.html). The sequence type (ST) of the isolate was ST101.

Blood culture test results for this patient upon admission were negative. The patient responded well to empiric treatment with 750 mg/day of levofloxacin and 1000 mg/day of metronidazole. Although the liver abscess was not drained, based on the clinical response to levofloxacin, OXA-48-producing K. pneumoniae was thought to be only colonizing organism, which was not contributing to the infectious clinical syndrome in this patient. He was discharged 21 days after arrival.

To our knowledge, this is the second case of isolation of OXA-48-producing K. pneumoniae in Japan. The first involved a man who had been hospitalized in a
Southeast Asian country. Multidrug-resistant (resistant to third and fourth generation cephalosporins, aminoglycosides, and quinolones; MIC of imipenem was 2 mg/L) *K. pneumoniae* and *E. coli* were isolated from the sputum and/or feces, and PCR analyses of the carbapenemase genes revealed the presence of a *blaOXA-48*-like gene in these isolates (9).

Our patient had traveled to Turkey and received medical care at an ICU in Egypt. OXA-48-producing organisms have been reported in both countries (14). The patient had no other history of travel to a foreign country for 1 year prior to this episode; therefore, it is likely that he acquired OXA-48-producing *K. pneumoniae* while receiving medical care at the ICU in Egypt. Drug-resistant *K. pneumoniae* ST101 has been reported as a causative agent of outbreaks or as a predominant clone of nosocomial pathogens in medical settings in several Mediterranean countries, including Greece (15), Italy (16,17), Libya (18), and Spain (19). The isolate from our patient was identified as ST101 by MLST, and thus, it was considered not to be of the K1 serotype, which is associated with liver abscess (20).

Of particular concern, OXA-48 carbapenemase-producing organisms may not necessarily be reported as carbapenem-resistant based on the MIC, as most microbiology laboratories in Japan continue to use the former CLSI criteria, in which *Enterobacteriaceae* samples with an MIC for imipenem of ≤4 mg/L are categorized as susceptible to carbapenem (10). Clinical isolates that show resistance to third generation cephalosporins and/or other classes of antibiotics (e.g., aminoglycoside and quinolone) and reduced susceptibility (MIC >1 mg/L) to carbapenems should be carefully considered and analyzed. Screening for carbapenemase and the modified Hodge test and PCR analyses for such isolates is strongly recommended.

For patients at potential risk of infection, such as those with a history of hospitalization abroad, a proactive approach is necessary to control the spread of MRDs. Thus, screening of all patients with a history of hospitalization abroad, as well as those transferred from other hospitals and nursing homes, should be considered.

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**Conflict of interest** None to declare.

**REFERENCES**
