Letter to the Editor
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The First *Klebsiella pneumoniae* Isolate Co-Producing OXA-48 and NDM-1 in Turkey

Abdullah Kilic, M.D. and Mehmet Baysallar, M.D.

Department of Clinical Microbiology, School of Medicine, Gulhane Military Medical Academy, Ankara, Turkey

Dear Editor

Resistance to broad-spectrum antimicrobials is a well-known challenge in treating *Enterobacteriaceae* infection worldwide. Carbapenems are an important class of antimicrobials used in treatment against these organisms, although increasing resistance to carbapenems has been reported among *Enterobacteriaceae* [1].

The production of OXA-48 was first described in *Klebsiella pneumoniae* isolates from Istanbul [2]. Although most reports describe single cases [3], important outbreaks have also been reported. *K. pneumoniae* and other *Enterobacteriaceae* strains with OXA-48 carbapenemase are now spreading from the Middle East to Europe, Asia, and North America. In addition, NDM-1 (another carbapenemase) was first identified in a *K. pneumoniae* isolate from a Swedish patient who had been treated in India in 2009 [4]. NDM-1 has since been reported in numerous isolates, predominantly in *Escherichia coli* and *K. pneumonia*, in many countries, including the United Kingdom, India, Pakistan, and Bangladesh [1].

Between June 2010 and May 2013, we collected 887 *Enterobacteriaceae* isolates from patients who were admitted to the Gulhane Military Medical Academy. All isolates were tested for susceptibility to 19 antimicrobials by using the Phoenix System (Becton Dickinson Diagnostic Systems, Sparks, MD, USA), and the test results were interpreted by using the CLSI criteria. The Modified Hodge test (MHT) was used to screen for the production of carbapenemase, and carbapenem-resistant isolates were examined by using real-time polymerase chain reaction for the expression of bla_{KPC}, bla_{NDM-1}, and bla_{OXA-48} [5, 6]. The nucleotide sequences were then analyzed by using an Applied Biosystems sequencer (ABI Prism 310 genetic analyzer; PE Applied Biosystems, Foster City, CA, USA). Multiple alignments were performed by using DNAMAN 4.1 software (Lynnon BioSoft, Québec, Canada) for isolates producing NDM-1.

Forty-nine of the 887 *Enterobacteriaceae* isolates (5.52%) were resistant to ≥1 of the three carbapenems (imipenem, meropenem, and ertapenem), and MHT revealed that all 49isolates were strong carbapenemase producers. No isolates harbored bla_{KPC}, although 48 harbored bla_{OXA-48}, and 1 *K. pneumoniae* isolate that was recovered from a patient's urine sample was positive for both bla_{OXA-48} and bla_{NDM-1}. This patient was a 75-yr-old woman who was living in Sanliurfa (on the southeastern border of Turkey) and was diagnosed as having chronic obstructive pulmonary disease, pneumonia, and hypotension. In 2013, she was transferred to the Pulmonary Diseases Department of a hospital in the central region of Turkey with severe shortness of breath, sluggishness, reduced consciousness, and weakness in her legs and arms. On the day after her admission, she developed severe respiratory fail-

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Corresponding author: Abdullah Kilic
Department of Clinical Microbiology, School of Medicine, Gulhane Military Medical Academy, 06018, Etlik, Ankara, Turkey
Tel: +90-312-3043412, Fax: +90-312-3042700, E-mail: abkilic@gata.edu.tr

ure and was transferred to the intensive care unit. *Acinetobacter* sp. had been isolated from her sputum in the Sanliurfa hospital, and she was receiving colistin and sulbactam when she was admitted to our hospital. Unfortunately, her condition deteriorated over the first three days of her admission, despite the antibiotic treatment. She subsequently developed sudden cardiac arrest, and resuscitation was unsuccessfully attempted. Culture of a urine sample (taken two days after her admission) revealed a *K. pneumoniae* isolate that was resistant to imipenem, meropenem, all β-lactams, all aminoglycosides, fluoroquinolones, nitrofurantoin, chloramphenicol, trimethoprim-sulfamethoxazole, and colistin. Interestingly, the isolate was susceptible to tigecycline only (minimum inhibitory concentration <1 mg/L).

Dissemination of *K. pneumoniae* isolates harboring carbapenemase resistance genes continues unrelieved. NDM-1 or OXA-48 positive *K. pneumoniae* isolates have been identified worldwide. However, *K. pneumoniae* positive for both NDM-1 and OXA-48 have been reported yet in only three cases around the world. The first *K. pneumoniae* strain co-producing NDM-1 and OXA-48 was isolated from an elderly male's urine sample in Morocco [7]. The second one was reported in Tunisia, a country where OXA-48 producers are already endemic as in Turkey [8]. And the third one was detected in the screening rectal swab of a patient transferred from the intensive care unit of a hospital located in Belgrade of Serbia to Bern University Hospital in Switzerland [9].

Here, we report the forth *K. pneumoniae* isolate that co-produced the OXA-48 and NDM-1 carbapenemases, which was obtained from a patient who was transferred from Sanliurfa (on the border between Syria and Ankara). To our knowledge, such a case has never been reported in Turkey to date. Due to the Syrian civil war, more than 600,000 persons have immigrated to Turkey and are living in refugee camps that were built in the Turkish border cities. In addition, many injured civilians have been transferred to the Sanliurfa hospital for treatment. Interestingly, NDM-1-producing *Acinetobacter baumannii* has already been isolated in a Lebanon hospital from Syrian patients who were wounded during the civil war [10].

In conclusion, Syria may be a source of NDM-1 producing isolates, along with Iraq [11], and these isolates may be spread to Turkey via individuals injured in civil war or Syabrian refugees. The emergence of NDM-1-producing *Enterobacteriaceae* isolates is a major health concern, and it highlights the need for further surveillance in this area.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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