AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

LETTER TO THE EDITOR

Emergence of Plasmid-Mediated Colistin Resistance Gene *mcr-1* in a Clinical *Escherichia coli* Isolate from Egypt

Shimaa S. Elnahriry,[a,b] Hazim O. Khalifa,[a,c] Ahmed M. Soliman,[a] Ashraf M. Ahmed,[a,d] Alaaddin M. Hussein,[b] Toshi Shimamoto,[a] Tadashi Shimamoto[a]

Laboratory of Food Microbiology and Hygiene, Graduate School of Biosphere Science, Hiroshima University, Higashi-Hiroshima, Japan[a]; Department of Bacteriology, Mycology and Immunology, Faculty of Veterinary Medicine, University of Sadat City, Sadat City, Egypt[b]; Department of Pharmacology, Faculty of Veterinary Medicine, Kafrelsheikh University, Kafr El-Sheikh, Egypt[c]; Department of Bacteriology, Mycology and Immunology, Faculty of Veterinary Medicine, Kafrelsheikh University, Kafr El-Sheikh, Egypt[d]

Colistin is considered a last resort for the treatment of infections caused by carbapenemase-producing members of the family *Enterobacteriaceae*. Recently, a transferable plasmid conferring resistance to colistin was discovered in *Escherichia coli* and *Klebsiella pneumoniae* from China (1) and was then reported in various bacteria from many other countries (2–4). This spread of antibiotic resistance heralds a return to the preantibiotic era, especially with no new antibiotics in the pipeline.

The plasmid-mediated colistin resistance gene *mcr-1* has been identified mainly in bacterial species from animals and animal products (pork and chicken meat) (1, 2). However, it was also detected in humans, i.e., patients (1–4), asymptomatic people (5), and some people by whom it was community acquired (6). Therefore, we used PCR and DNA sequencing to screen for the presence of *mcr-1* in 241 nonduplicate Gram-negative clinical bacterial isolates collected from hospitals in different cities in Egypt during 2015. A universal primer pair, CLR5-F (5′-CGGTCAGTCCGTTTGTTC-3′) and CLR5-R (5′-CTTGGTCGGTCTGTAGGG-3′), was used for screening as previously described (1). In addition, the entire *mcr-1* region was amplified and sequenced with MCR-1-F2 (5′-CTCATGATGCAGCATACTTC-3′) and MCR-1-R2 (5′-CGAATGGAGTGTGCGGTG-3′), which were based on the consensus sequences that flank *mcr-1* (GenBank accession no. KP347127). Analysis showed that *mcr-1* was present in only one *E. coli* isolate (SP-1), which was from the sputum of a patient with bacteremia who was hospitalized in the intensive care unit of a Cairo City hospital with no history of traveling abroad. The MIC of both colistin and polymyxin B for this isolate was 16 mg/liter.

E. coli SP-1 had phenotypic resistance to colistin, ciprofloxacin, nalidixic acid, kanamycin, tetracycline, chloramphenicol, ceftriaxone, ampicillin, and cefotaxime but was susceptible to carbapenems. Multilocus sequence typing (MLST) indicated that *E. coli* SP-1 belonged to sequence type 1011 (ST1011), which differed from sequence types identified for clinical *E. coli* isolates harboring *mcr-1* in Denmark (ST744) (2) and Cambodia (ST354) (3). According to the MLST database (http://mlst.ucc.ie/mlst/mlst/dbs/Ecoli), *E. coli* ST1011 was reported in humans in Egypt and in cats and swine in Germany. Of note, *E. coli* ST1011 was detected previously as an avian fecal *E. coli* strain in Egypt (7) and it was found to be shared by avian pathogenic *E. coli* and human extraintestinal pathogenic *E. coli* by phylogenetic grouping in Brazil (8). Also, it was found as CTX-M-64-harboring *E. coli* isolates from chickens in China (9). Therefore, *E. coli* ST1011 may have potential zoonotic importance.

Southern hybridization showed that *mcr-1* was located on a plasmid of >90 kb. This plasmid was successfully transferred to *E. coli* J53 recipient cells through conjugation. The presence of *mcr-1* in the transconjugants was confirmed by PCR. Of note, *E. coli* SP-1 also contained $bla_{\text{CTX-M-15}}$ and a class 1 integron (*dfrA12-orfF-aadA2*). $bla_{\text{CTX-M-15}}$ was also detected in an *mcr-1*-positive *E. coli* isolate from the Netherlands (3).

In conclusion, this study is the first report of *mcr-1* in a clinical human isolate from Egypt and even the entire African continent. This report confirms other reports of the alarming spread of the plasmid-mediated gene *mcr-1*. We can ultimately find ourselves facing pandrug resistance in members of the family *Enterobacteriaceae*. The high prevalence of *mcr-1* in animal isolates compared with human clinical isolates worldwide suggests that animals and their products are potential sources of *mcr-1* in humans. The misuse of colistin in agriculture and the poultry industry may be the main cause of the high incidence of *mcr-1* in bacteria from animals and animal products. This issue should be addressed by all appropriate authorities by banning the careless use of colistin in agriculture.

Nucleotide sequence accession number. The nucleotide sequence of the *mcr-1* gene was submitted to DDBJ/EMBL/GenBank and assigned accession no. LC114018.

ACKNOWLEDGMENTS

S.S.E. is supported by a doctoral fellowship (channel system) from the Ministry of Higher Education, Egypt. H.O.K. was supported by a doctoral fellowship from the Ministry of Higher Education, Egypt. A.M.A. is supported by a postdoctoral fellowship (no. PU14012) from the Japan Society for the Promotion of Science. This work was supported by grants-in-aid for scientific research (no. 25460532 and 26.04912) to Tadashi Shimamoto from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

FUNDING INFORMATION

This work, including the efforts of Tadashi Shimamoto, was funded by Ministry of Education, Culture, Sports, Science, and Technology (MEXT) (25460532). This work, including the efforts of Tadashi Shimamoto, was funded by Ministry of Education, Culture, Sports, Science, and Technology (MEXT) (26.04912).

REFERENCES

1. **Liu YY, Wang Y, Walsh TR, Yi L-X, Zhang R, Spencer J, Doi Y, Tian G, Dong B, Huang X, Yu LF, Gu D, Ren H, Chen X, Lv L, He D, Zhou H,**

Accepted manuscript posted online 7 March 2016

Citation Elnahriry SS, Khalifa HO, Soliman AM, Ahmed AM, Hussein AM, Shimamoto T, Shimamoto T. 2016. Emergence of plasmid-mediated colistin resistance gene *mcr-1* in a clinical *Escherichia coli* isolate from Egypt. Antimicrob Agents Chemother 60:3249–3250. doi:10.1128/AAC.00269-16.

Address correspondence to Tadashi Shimamoto, tadashis@hiroshima-u.ac.jp.

Copyright © 2016, American Society for Microbiology. All Rights Reserved.

Liang Z, Liu JH, Shen J. 2016. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect Dis **16:**161–168. http://dx.doi.org/10.1016/S1473-3099(15)00320-5.

2. **Hasman H, Hammerum AM, Hansen F, Hendriksen RS, Olesen B, Agersø Y, Skov RL.** 2015. Detection of *mcr-1* encoding plasmid-mediated colistin-resistant *Escherichia coli* isolates from human bloodstream infection and imported chicken meat, Denmark 2015. Euro Surveill **20**(49). http://dx.doi.org/10.2807/1560-7917.ES.2015.20.49.30085.
3. **Stoesser N, Mathers AJ, Moore CE, Day NP, Crook DW.** 2016. Colistin resistance gene *mcr-1* and pHNSHP45 plasmid in human isolates of *Escherichia coli* and *Klebsiella pneumoniae*. Lancet Infect Dis **16:**285–286. http://dx.doi.org/10.1016/S1473-3099(16)00010-4.
4. **Falgenhauer L, Waezsada SE, Yao Y, Imirzalioglu C, Käsbohrer A, Roesler U, Chakraborty T, RESET Consortium.** 2016. Colistin resistance gene *mcr-1* in extended-spectrum β-lactamase-producing and carbapenemase-producing Gram-negative bacteria in Germany. Lancet Infect Dis **16:**282–283. http://dx.doi.org/10.1016/S1473-3099(16)00009-8.
5. **Arcilla MS, van Hattem JM, Matamoros S, Melles DC, Penders J, de Jong MD, Schultsz C.** 2016. Dissemination of the *mcr-1* colistin resistance gene. Lancet Infect Dis **16:**147–149. http://dx.doi.org/10.1016/S1473-3099(15)00541-1.
6. **Olaitan AO, Chabou S, Okdah L, Morand S, Rolain JM.** 2016. Dissemination of the *mcr-1* colistin resistance gene. Lancet Infect Dis **16:**147. http://dx.doi.org/10.1016/S1473-3099(15)00540-X.
7. **Hussein AH, Ghanem IA, Eid AA, Ali MA, Sherwood JS, Li G, Logue CM.** 2013. Molecular and phenotypic characterization of *Escherichia coli* isolated from broiler chicken flocks in Egypt. Avian Dis **57:**602–611. http://dx.doi.org/10.1637/10503-012513-Reg.1.
8. **Maluta RP, Logue CM, Casas MRT, Meng T, Guastalli EAL, Rojas TCG, da Silveira WD.** 2014. Overlapped sequence types (STs) and serogroups of avian pathogenic (APEC) and human extra-intestinal pathogenic (ExPEC) *Escherichia coli* isolated in Brazil. PLoS One **9:**e105016. http://dx.doi.org/10.1371/journal.pone.0105016.
9. **Liu C.** 2014. Molecular epidemiology of hybrid CTX-M type beta-lactamases. M.S. thesis. University of Hong Kong.