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# Co-production of MCR-1 and extended-spectrum β-lactamase in *Escherichia coli* recovered from urinary tract infections in Switzerland

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Sir,

The recent identification of the transferable colistin resistance genes *mcr-1* and *mcr-2* represents an additional step towards the occurrence of pandrug-resistant enterobacterial strains [1]. MCR-1 and MCR-2-producing Enterobacteriaceae are mainly recovered from animals, and particularly from pigs. Conversely, rare occurrence of MCR-1 and MCR-2-producers has been described from clinical samples and the environment [2]. In Switzerland, several screening studies showed a low prevalence of MCR-1 and MCR-2 producers in clinical isolates recovered from blood culture and urines [3, 4]. Here we report two cases of urinary tract infections associated with *Escherichia coli* isolates co-producing an extended-spectrum β-lactamase (ESBL) and the polymyxin resistance determinant MCR-1, recovered from patients hospitalized at the hospital of Neuchâtel, Switzerland.

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The first patient was an 83-year-old man who presented a urinary tract infection caused by *E. coli* following the urological surgery in December 2015. The *E. coli* isolate (CDF-6) showed resistance to broad-spectrum cephalosporins, and the patient was therefore treated by ertapenem for ten days. The second patient was a 75-year-old man who was admitted for the treatment of an adenocarcinoma in January 2016, and had a nephrostomy due to a renal failure. He presented a first urinary tract infection caused by a *Proteus mirabilis* isolate. After treatment by cefuroxime for 14 days, an *E. coli* isolate showing resistance to broad-spectrum cephalosporins (CDF-8) was recovered from urine. None of those patients received prior treatment with polymyxin, nor traveled abroad.

Both isolates were tested for colistin resistance with the Rapid Polymyxin NP® test (ELITech, Signes, France) and were found positive after 2 h of incubation. Disk diffusion susceptibility testing performed on Muller–Hinton (MH) agar (Bio-Rad, Cressier, Switzerland) showed that both isolates exhibited an ESBL profile. Minimal inhibitory concentrations (MICs) were determined using the broth microdilution method using cation-adjusted MH broth (Bio-Rad) and both isolates showed an MIC of colistin at 8 µg/ml. PCR amplifications followed by sequencing detected the *mcr-1* gene in both isolates. In addition, the isolates were positive for the $bla_{\text{CTX-M-1}}$ and $bla_{\text{CTX-M-15}}$ ESBL encoding genes, respectively. Multilocus sequence types were determined by amplification and sequencing of seven housekeeping genes, and sequence types were assigned using the Warwick *E. coli* MLST database (http://mlst.warwick.ac.uk/mlst/dbs/Ecoli). Phylogenetic groups were determined by the PCR-based Clermont method consisting in the detection of specific virulence genes. Isolates CDF-6 and CDF-8 belonged to ST446 and ST164, respectively, and to the commensal B1 and C phylogenetic groups, respectively. Conjugation followed by PCR-based replicon typing analyzes and plasmid

extractions showed that the *mcr-1* gene was located on a ca. 250-kb IncHI2 and ca. 33-kb IncX4 plasmids for the CDF-6 and CDF-8 isolates, respectively. Resistance to sulfamethoxazole/trimethoprim and tetracycline was co-transferred with the IncHI2-carrying *mcr-1* plasmid, whereas no co-resistance was found to be associated with the IncX4-carrying *mcr-1* plasmid. Additionally, two full copies of the insertion sequence IS*Apl1* bracketing the *mcr-1* gene were identified on the IncHI2 plasmid, forming transposon Tn*6330* [5].

That study reports on two likely community-acquired *E. coli* isolates co-producing MCR-1 and a CTX-M-like β-lactamase. These isolates belonged to different sequence types and were not related to extra-intestinal pathogenic strains. Noteworthy, previous studies reported ST446 and ST164 *E. coli* from animal samples including poultry, swine and cattle, strengthening the likelihood of an animal origin for those strains. Rapid detection of colistin resistance has beneficiated from the use of the Rapid Polymyxin NP test that takes 2 h of incubation, whereas MIC determinations usually take 18 h. Noteworthy, both patients did not receive previous polymyxin-based treatments, suggesting a hidden circulation of those strains.

**Compliance with ethical standards**

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**Conflict of interest** The authors declare that they have no conflict of interest.

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