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Multiple colonization with highly resistant bacteria: carbapenemase-producing Enterobacteriaceae, carbapenemase-producing *Pseudomonas aeruginosa*, carbapenemase-producing *Acinetobacter baumannii*, and glycopeptide-resistant *Enterococcus faecium*

To the Editors,

The dissemination of carbapenemase-producing bacteria worldwide is an important source of concern because carbapenemase producers are multidrug resistant (Nordmann and Poirel, 2014). National guidelines increasingly recommend a systematic screening of at least carbapenemase-producing Enterobacteriaceae (CPE) and glycopeptide-resistant enterococci (GRE) in patients admitted to hospitals who have been hospitalized aboard during the preceding 12 months (Lepelletier et al., 2011). We have investigated the occurrence of colonization and infection with multiple highly resistant bacteria of more than 4 different genus in 2 patients directly transferred from a foreign country.

In June 2014, a 33-year-old French man (patient A) was admitted for a suicide attempt in a Vietnamese hospital where he was treated during 10 days for pneumonia with piperacillin + tazobactam before his transfer to Necker-Enfants Malades University Hospital in Paris, France. At the day of his hospitalization in France, distal protected pulmonary samples were collected, and imipenem was administered subsequently to a persistent fever. In addition, systematic screening to detect carbapenemase producers and GRE was also performed. Screening of extended spectrum β-lactamase (ESBL) producing Enterobacteriaceae, carbapenemase producers, and GRE was done on selective media (bioMérieux, La Balme-les-Grottes, France) ChromID ESBL, ChromID Carba Smart, and VRE medium, respectively. Carbapenemase production was identified using the Carba NP test for Enterobacteriaceae (Dortet et al., 2014a) and *Pseudomonas aeruginosa* (Dortet et al., 2012) and CarbAcineto NP test for *Acinetobacter baumannii* (Dortet et al., 2014b). Definitive identifications of resistance determinant were done by PCR amplifications followed by sequencing. Pulmonary samples grew an OXA-23–producing *A. baumannii* isolate and an IMP-1–producing *P. aeruginosa* (Table 1). Screening identified also that the patient was colonized with a KPC-2–producing *Klebsiella pneumoniae*, a CTX-M-15–producing *K. pneumoniae*, and a VanA-positive glycopeptide-resistant *Enterococcus faecium* (Table 1).

Patient B was a 66-year-old French woman who was hospitalized in May 2014 in the intensive care unit of Paris suburb (Saint-Denis, France). She was directly transferred from Morocco, where she was admitted in the intensive care unit consecutively to a road accident. Seven days after her admission, she developed a ventilation-associated pulmonary infection due to a multidrug-resistant *P. aeruginosa* that was treated with imipenem, colistin, metronidazole, and fluconazole for 14 days. Twenty-one days after the admission, the patient developed another pulmonary infection due to a multidrug-resistant *A. baumannii* only susceptible to colistin, resulting in her transfer to the French hospital. At the admission, the systematic screening of CPE using rectal swab samples revealed the presence of an OXA-48–producing *K. pneumoniae* (Table 1). After 24 hours, the patient developed a pyelonephritis due to a VIM-4–producing *P. aeruginosa* and a bronchitis due to an OXA-23–producing *A. baumannii* (Table 1), which were treated with amikacin, fosfomycin, and colistin. Although apyrexia was

Table 1
Clinical data on the 2 patients hospitalized in France after hospitalization in another country and were carrying multidrug-resistant bacteria.

Patient	Country of initial hospitalization	Species	Clinical sample	β-Lactamase content[a]	Non–β-lactam resistance determinants
A	Vietnam	*A. baumannii*	PDP	**OXA-23**	ArmA
		P. aeruginosa	PDP	**IMP-1**	
		K. pneumoniae	Rectal swab	**KPC-2**, CTX-M-15, TEM-1, SHV-1, OXA-1	AAC6′-Ib-cr, QnrB
		K. pneumoniae	Rectal swab	CTX-M-15, TEM-1, SHV-1, OXA-1	AAC6′-Ib-cr, QnrB
		E. faecium	Rectal swab	None	VanA
B	Morocco	*A. baumannii*	PDP	**OXA-23**	
		P. aeruginosa	Urine and blood culture	**VIM-4**	
		P. rettgeri	Urine	**NDM-1**, CTX-M-15, SHV-12, TEM-1,	AAC6′-Ib-cr, QnrB
		K. pneumoniae	Rectal swab	**OXA-48**, CTX-M-15, OXA-9	AAC6′-Ib-cr, QnrB

PDP = distal protected pulmonary sample.
[a] Carbapenemase are in boldface; ESBL are underlined.

obtained in 3 days, fever reappeared under colistin treatment. A naturally colistin-resistant *Providentia rettgeri* isolate producing the NDM-1 carbapenemase was isolated from 3 successive urine samples recovered by urinary catheter (Table 1). The urinary catheter was removed, and the patient received 2 doses of amikacin, leading to a rapid apyrexia.

Co-occurrence of multiple resistance determinants in the same species has become a common feature among carbapenemase producers (Compain et al., 2014). Nevertheless, co-occurrence in the same patient of a least 4 different highly resistant bacterial species is worrisome because it might potentially lead to a real therapeutic deadlock.

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Delphine Girlich
Faculty of Medecine, South-Paris University, Le Kremlin-Bicêtre, France

Patrice Nordmann
INSERM U914 « Emerging Resistance to Antibiotic »
Le Kremlin-Bicêtre, France
Associated National Reference Center to Antibiotic
Resistance, Le Kremlin-Bicêtre, France
Medical and Microbiology Unit, Department of Medecine
University of Fribourg, Fribourg, Switzerland
Hôpital Fribourgeois-hôpital Cantonal, Fribourg, Switzerland

Hervé Lécuyer
Patrick Berche
Bacteriology-Virology-Hygiene unit, Necker-Enfants Malades Hospital
Assistance Publique / Hôpitaux de Paris, Paris, France

Anne Marmorat-Khuong
Isabelle Gros
Centre Hospitalier de Saint-Denis
Saint-Denis, France

Gaëlle Cuzon
Bacteriology-Hygiene unit, Bicêtre Hospital
Assistance Publique / Hôpitaux de Paris, Le 11 Kremlin-Bicêtre, France
INSERM U914 « Emerging Resistance to Antibiotic »
Le Kremlin-Bicêtre, France
Associated National Reference Center to Antibiotic
Resistance, Le Kremlin-Bicêtre, France

Laurent Dortet
Faculty of Medecine, South-Paris University, Le Kremlin-Bicêtre, France
Bacteriology-Hygiene unit, Bicêtre Hospital
Assistance Publique / Hôpitaux de Paris, Le Kremlin-Bicêtre, France
INSERM U914 « Emerging Resistance to Antibiotic »
Le Kremlin-Bicêtre, France
Associated National Reference Center to
Antibiotic Resistance, Le Kremlin-Bicêtre, France
Corresponding author. Mailing address: Service de Bactériologie-Virologie, Hôpital de Bicêtre, 78 rue du Général Leclerc, 94275 Le Kremlin-Bicêtre Cedex, France
E-mail address: laurent.dortet@bct.aphp.fr

References

Compain F, Decre D, Frazier I, Ramahefasolo A, Lavollay M, Carbonnelle E, et al. Carbapenemase-producing bacteria in patients hospitalized abroad, France. Emerg Infect Dis 2014;20:1246–8.

Dortet L, Poirel L, Nordmann P. Rapid detection of carbapenemase-producing *Pseudomonas* spp. J Clin Microbiol 2012;50:3773–6.

Dortet L, Brechard L, Poirel L, Nordmann P. Impact of the isolation medium for detection of carbapenemase-producing *Enterobacteriaceae* using an updated version of the Carba NP test. J Med Microbiol 2014a;63:772–6.

Dortet L, Poirel L, Errera C, Nordmann P. CarbAcineto NP test for rapid detection of carbapenemase-producing *Acinetobacter* spp. J Clin Microbiol 2014b;52:2359–64.

Lepelletier D, Andremont A, Grandbastien B, National Working G.. Risk of highly resistant bacteria importation from repatriates and travelers hospitalized in foreign countries: about the French recommendations to limit their spread. J Travel Med 2011;18:344–51.

Nordmann P, Poirel L. The difficult-to-control spread of carbapenemase producers among *Enterobacteriaceae* worldwide. Clin Microbiol Infect 2014;20:821–30.