NDM-1-Producing *Acinetobacter baumannii* from Algeria

Over the last decade, nosocomial infections with *Acinetobacter baumannii* have been described with an increasing trend toward multidrug resistance, mostly in intensive care units (ICUs) (6, 9, 11). The main mechanism of resistance to carbapenems in *A. baumannii* is the production of acquired OXA-type carbapenemases, which have been frequently identified worldwide and are clustered in three major subfamilies (*bla*_{OXA-23}, *bla*_{OXA-24}, and *bla*_{OXA-58}), and more rarely metallo- β -lactamases (VIM, IMP, and SIM types), which have been sporadically reported in some parts of the world (6, 9, 10, 11). A novel metallo- β -lactamase, NDM-1, that recently emerged first in *Klebsiella pneumoniae* and *Escherichia coli*, represents a significant resistance trait (7, 8). Several *A. baumannii* isolates expressing NDM variants have been detected in India, and recent studies reported NDM-producing *A. baumannii* in China, Germany, Egypt, Oman, and Israel (2–4). Here we report the first NDM-1-producing *A. baumannii* isolate from Algeria.

A 25-year-old man previously hospitalized in the ICU of the hospital of Oran, Algeria, for severe cranial trauma subsequent to a traffic accident was transferred to the ICU of the Bicêtre hospital in July 2011. At admission, cultures from a blood catheter and from rectal swabs revealed carbapenem-resistant *A. baumannii* strain Ora-1. During the same period of time, no other *A. baumannii* isolate was recovered from the Bicêtre hospital.

Species identification and susceptibility testing (disk diffusion and Etest) were performed as previously described (1, 5, 6). *A. baumannii* Ora-1 was susceptible to amikacin, netilmicin, tigecycline, rifampin, and colistin and resistant to all of the β -lactams, including carbapenems, with imipenem and meropenem MICs of >32 $\mu\text{g/ml}$ that are antagonized by the addition of EDTA (Table 1), as determined using the Etest method.

A crude β -lactamase extract of *A. baumannii* Ora-1 prepared as previously described, in phosphate buffer supplemented with 50 mM ZnCl_2 (3), had very weak imipenem hydrolysis activity (specific activity = 8.6 mU/mg, only 3-fold above the background obtained with an imipenem-susceptible isolate), compatible with

OXA carbapenemase expression (6, 10, 11). Most of the acquired Ambler class A, class B, and class D β -lactamase genes; the naturally occurring *bla*_{AmpC} and *bla*_{OXA-51}-like genes; and the 16S rRNA methylase-encoding genes (*armA*, *rmtA*, *rmtB*, *rmtC*, *rmtD*, and *npmA*) were sought by PCR followed by sequencing. Only *bla*_{NDM-1} and the chromosomally encoded *bla*_{AMPC} and *bla*_{OXA-94} genes were identified. *ISAbal* was inserted upstream of the *bla*_{AMPC} gene, likely resulting in its overexpression (6, 11). Analysis of the genetic environment of the *bla*_{NDM-1} gene by PCR revealed *ISAbal25* present on both sides of the *bla*_{NDM-1} gene, forming a composite transposon (2).

Conjugation and electroporation experiments using azide-resistant *E. coli* J53 or rifampin-resistant *A. baumannii* CIP7010 as the recipient were unsuccessful (data not shown) (6). Plasmid extractions revealed the presence of a plasmid of >150 kb that did not hybridize with a *bla*_{NDM-1}-specific probe (3), suggesting that the *bla*_{NDM-1} gene is likely to have a chromosomal location, as described for other NDM-producing *A. baumannii* isolates (3, 4, 6).

The identification of a *bla*_{NDM-1} gene in a clinical *A. baumannii* isolate originating from Algeria, with no obvious link with the Indian subcontinent, suggests that NDM-producing *A. baumannii* isolates may have spread already in North Africa. Only molecular tools were capable of detecting NDM in *A. baumannii*, and it is likely that carbapenem resistance is the result of decreased production of outer membrane porins, together with low-level expression of NDM (6, 11). Finally, these results highlight the importance of international patient transfer as a source of dissemination of antimicrobial resistance.

Published ahead of print 30 January 2012

Address correspondence to Thierry Naas, thierry.naas@bct.aphp.fr.

Copyright © 2012, American Society for Microbiology. All Rights Reserved.

doi:10.1128/AAC.05653-11

TABLE 1 MICs of various antibiotics for *A. baumannii* Ora-1

Isolate	MIC ($\mu\text{g/ml}$) ^a										
	TIC	CTX	CAZ	ATM	IPM	IPM + EDTA	MEM	DOR	CS	TGC	RA
<i>A. baumannii</i> Ora-1 ^b	>256	>256	>256	>256	>32	<1	>32	>32	1	1	2

^a TIC, ticarcillin; CTX, cefotaxime; CAZ, ceftazidime; ATM, aztreonam; IPM, imipenem; IPM + EDTA, imipenem supplemented with EDTA; MEM, meropenem; DOR, doripenem; CS, colistin; TGC, tigecycline; RA, rifampin; AN, amikacin.

^b The β -lactamase genes that were sought by PCR were *bla*_{NDM}, *bla*_{IMP}, *bla*_{VIM}, *bla*_{SIM}, *bla*_{OXA-23}, *bla*_{OXA-40}, *bla*_{OXA-58}, *bla*_{OXA-143}, *bla*_{OXA-51}, *bla*_{TEM}, and *bla*_{AMPC}. Only signals for *bla*_{NDM}, *bla*_{OXA-51}, and *bla*_{AMPC} were positive.

ACKNOWLEDGMENTS

We are grateful to Winchygn Liu, Anaïs Potron, and Remy Bonnin for technical assistance.

The research leading to these results has received funding from INSERM, from the Ministère de l'Éducation Nationale et de la Recherche (UPRES-EA3539), and from the European Community's Seventh Framework Programme FP7/2010-2013 under grant agreement no. 241742 (TEMPOtest-QC).

We have no conflicts of interest to declare.

REFERENCES

1. Clinical and Laboratory Standards Institute. 2010. Performance standards for antimicrobial susceptibility testing: twentieth informational supplement M100-S20-U. Clinical and Laboratory Standards Institute, Wayne, PA.
2. Espinal P, et al. 2011. Dissemination of an NDM-2-producing *Acinetobacter baumannii* clone in an Israeli rehabilitation center. *Antimicrob. Agents Chemother.* 55:5396–5398.
3. Kaase M, et al. 2011. NDM-2 carbapenemase in *Acinetobacter baumannii* from Egypt. *J. Antimicrob. Chemother.* 66:1260–1262.
4. Karthikeyan K, Thirunarayan MA, Krishnan P. 2010. Coexistence of blaOXA-23 with blaNDM-1 and armA in clinical isolates of *Acinetobacter baumannii* from India. *J. Antimicrob. Chemother.* 65:2253–2254.
5. Naas T, et al. 2006. VEB-1 extended-spectrum beta-lactamase-producing *Acinetobacter baumannii*, France. *Emerg. Infect. Dis.* 12:1214–1222.
6. Naas T, Nordmann P. 2009. *Acinetobacter* and β -lactams, p. 407–420. In Courvalin P, LeClerc R, Rice LB (ed), *Antibiogram*, 3rd ed. ASM Press, Washington, DC.
7. Nordmann P, Naas T, Poirel L. 2011. Global spread of carbapenemase-producing Enterobacteriaceae. *Emerg. Infect. Dis.* 17:1791–1798.
8. Nordmann P, Poirel L, Toleman MA, Walsh T. 2011. Does broad-spectrum β -lactam resistance due to NDM-1 herald the end of the antibiotic era for treatment of infections caused by Gram-negative bacteria? *J. Antimicrob. Chemother.* 66:689–692.
9. Perez F, et al. 2007. Global challenge of multidrug-resistant *Acinetobacter baumannii*. *Antimicrob. Agents Chemother.* 51:3471–3484.
10. Poirel L, Naas T, Nordmann P. 2010. Diversity, epidemiology and genetics of class D β -lactamases. *Antimicrob. Agents Chemother.* 54:24–38.
11. Poirel L, Nordmann P. 2006. Carbapenem resistance in *Acinetobacter baumannii*: mechanisms and epidemiology. *Clin. Microbiol. Infect.* 12: 826–836.

Anne Boulanger

Thierry Naas

Nicolas Fortineau

Service de Bactériologie-Virologie

Hopital de Bicetre, APHP

Université Paris XI

K.-Bicêtre, France

Samy Figueiredo

Département d'Anesthésie-Réanimation

Hôpital de Bicêtre, APHP

Université Paris XI

K.-Bicêtre, France

Patrice Nordmann

Inserm U914

Hopital de Bicetre, APHP

Faculté de Médecine Paris-Sud

K.-Bicêtre, France