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Case Report

First report of NDM-1-producing *Pseudomonas aeruginosa* in Egypt

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SUMMARY

This work reports the occurrence of New Delhi metallo-beta-lactamase 1 (NDM-1) in metallo-beta-lactamase-producing *Pseudomonas aeruginosa* in Egypt for the first time, and the presence of more than one *bla*MBL gene in carbapenem-resistant *P. aeruginosa*.

1. Introduction

New Delhi metallo-beta-lactamase 1 (NDM-1) has received wide attention because of the extreme resistance it confers, its presence in many common pathogens, its rapid spread to multiple continents, and local nosocomial spread in some areas. Most early reports of infections were in individuals who had received medical care in the Indian subcontinent.[1] The first variant of NDM-1 – NDM-2 – was detected in *Acinetobacter baumannii* from Egypt.[2] The acquisition of NDM-1 by two clinical isolates of metallo-beta-lactamase (MBL)-producing *Pseudomonas aeruginosa* in Egypt and the association of bla_{VIM-2} with the bla_{NDM-1} in these two isolates is reported herein.

2. Case report

The two *P. aeruginosa* isolates were recovered from hospitalized inpatients admitted to Kasr Al Aini Hospital, Cairo University, Egypt during March 2012. The first isolate was from a wound specimen obtained from a young man (23 years old) who had suffered 30% burns and was hospitalized in the surgical ward; he spent 10 days in the hospital. The second *P. aeruginosa* isolate was obtained from a sputum specimen recovered from a 74-year-old man who had a history of underlying malignancy (glioma) and who had undergone a brain tumor excision. He was hospitalized in the intensive care unit; he spent 22 days in the hospital. Both patients were alive after the hospitalization period.

The isolates were confirmed by VITEK 2 (bioMérieux, Marcy l'Etoile, France) and the minimum inhibitory concentrations (MICs) of selected antimicrobials were determined by Etest (AB Biodisk, Solna, Sweden). Both strains were resistant to imipenem and meropenem. The resistance patterns of both isolates are illustrated in Table 1.

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Table 1
Minimum inhibitory concentrations (Etest, μg/ml) for *Pseudomonas aeruginosa* clinical isolates

	Antibiotic								
	FEP	TZP	CAZ	CAZ/CLA	CIP	AMK	GEN	IPM	CTX
CLSI resistance break point	≥32	≥128/4	≥128/2	≥32	≥4	≥64	≥4	≥16	≥32
Wound	64	≥256	≥256	≥256	≥32	≥256	≥256	≥32	≥256
Sputum	24	≥256	≥256	192	≥32	≥256	12	≥32	≥256

FEP, cefepime; TZP, piperacillin/tazobactam; CAZ, ceftazidime; CAZ/CLA, ceftazidime/clavulanic acid; CIP, ciprofloxacin; AMK, amikacin; GEN, gentamicin; IPM, imipenem; CTX, cefotaxime.

Both isolates were positive for MBL production by combined disk test. PCRs with primers specific for $bla_{\text{VIM-2}}$ (AAAGTTATGCCG-CACTCACC and TGCAACTTCATGTTATGCCG)[3] and $bla_{\text{NDM-1}}$ (CACCT-CATGTTTGAATTCGCC and CTCTGTCACATCGAAATCGC)[2] revealed amplification of a 984-bp fragment corresponding to $bla_{\text{NDM-1}}$ and a fragment of 865 bp corresponding to the $bla_{\text{VIM-2}}$ gene. PCRs with primers specific for bla_{IMP} (5′-GAAGGYGTTTATGTTCATAC-3′ and 5′-GTAMGTTTCAAGAGTGATGC-3′), bla_{SPM} (5′-CTGCTTGGATT-CATGGGCGC-3′ and 5′-CCTTTTCCGCGACCTTGATC-3′), bla_{GIM} (5′-TCGACACACCTTGGTCTG-3′ and 5′-AACTTCCAACTTTGCCAT-3′), and bla_{SIM} (5′-TACAAGGGATTCGGCATCC-3′ and 5′-TAATGGCCTGTTCC-CATG-3′) genes were negative.[3,4]

Typing by multilocus sequence typing (MLST) of the recognized chromosomal markers (seven housekeeping genes) *acs*A, *aro*E, *gua*A, *mut*L, *nuo*D, *pps*A, and *trp*E (http://pubmlst.org/paeruginosa/) showed similarity in which sequence type (ST) 233, which is a part of the internationally dominant clonal cluster CC233, was detected in the two isolates.

3. Discussion

NDM-1-producers are now alarmingly on the increase worldwide and pose a potential risk for therapeutic failure with the empirical treatments currently in place.[5] The first identification of a bla_{NDM} gene in a clinical isolate originated from Egypt, with no obvious link to the Indian subcontinent.[2] Prior to the detection of the NDM-1-positive *P. aeruginosa* strains, neither of the patients in our study had traveled to the Indian subcontinent or any European country. Thus, either these patients experienced cross-transmission with NDM-1 cases that were travel-associated (but not reported), or inappropriate and non-prescription antibiotic use might have been the cause of the development of high antimicrobial resistance. The presence of $bla_{\text{VIM-2}}$ together with $bla_{\text{NDM-1}}$ in the two *P. aeruginosa* isolates reported in this study indicates the dissemination of *bla*MBL-carrying organisms in Egypt.

Typing by MLST of the two isolates revealed both to belong to ST233, indicating that health care-acquired transfer of *P. aeruginosa* could occur; an increased risk of cross-transmission and high antimicrobial pressure might have favored clonal spread. In addition, patients who have the potential to facilitate the dissemination of multidrug-resistant organisms between hospitals may subsequently serve as important reservoirs and transmission sources, stressing the importance of hand hygiene compliance and patient precautions.

In conclusion, this finding of NDM-1-producing *P. aeruginosa* and the presence of more than one *bla*MBL gene in carbapenem-resistant *P. aeruginosa* highlights the emerging therapeutic challenge. The implementation of strict antimicrobial policies and infection control programs may help to prevent the rapid dissemination of these organisms.

Conflict of interest: No conflict of interest to declare.

References

1. Wilson ME, Chen LH. NDM-1 and the role of travel in its dissemination. *Curr Infect Dis Rep* 2012;**14**:213–26.
2. Kaase M, Nordmann P, Wichelhaus TA, Gatermann SG, Bonnin RA, Poirel L. NDM-2 carbapenemase in *Acinetobacter baumannii* from Egypt. *J Antimicrob Chemother* 2011;**66**:1260–2.
3. Yan JJ, Hsueh PR, Ko WC, Luh KT, Tsai SH, Wu HM, et al. Metallo-β-lactamases in clinical pseudomonas isolates in Taiwan and identification of VIM-3, a novel variant of the VIM-2 enzyme. *Antimicrob Agents Chemother* 2001;**45**:2224–8.
4. Ellington M, Kistler J, Livermore D, Woodford N. Multiplex PCR for rapid detection of genes encoding acquired metallo-β-lactamases. *J Antimicrob Chemother* 2007;**59**:321–2.
5. Mulvey MR, Grant JM, Plewes K, Roscoe D, Boyd DA. New Delhi metallo-β-lactamase in *Klebsiella pneumoniae* and *Escherichia coli*, Canada. *Emerg Infect Dis* 2011;**17**:103–6.