First case of bacteraemia due to Acinetobacter schindleri harbouring blaNDM-1 in an immunocompromised patient

S. Montaña1, S. Palombarani2, M. Carulla3, A. Kunst4, C. H. Rodriguez4, M. Nastro4, C. Vay4, M. S. Ramirez5 and M. Almuzara2,4

1) Instituto de Microbiología y Parasitología Médica (IMPaM, UBA-CONICET), Facultad de Medicina, Universidad de Buenos Aires, 2) Laboratorio de Bacteriología, 3) Servicio de Infectología, Hospital Interzonal de Agudos Eva Perón, San Martín, Provincia de Buenos Aires, 4) Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Laboratorio de Bacteriología, Departamento de Bioquímica Clínica, Hospital de Clínicas José de San Martín, Ciudad Autónoma de Buenos Aires and 5) Center for Applied Biotechnology Studies, Department of Biological Science, California State University Fullerton, Fullerton, California, USA

Abstract

Clinically significant NDM-1-producing Acinetobacter schindleri has not yet been described in the literature. We report the first case of bacteraemia due to an A. schindleri strain harbouring blaNDM-1 recovered from an immunocompromised patient. Our report reinforces the fact that NDM-1 can easily be acquired by Acinetobacter species.

© 2017 The Author(s). Published by Elsevier Ltd.

Keywords: Acinetobacter schindleri, bacteraemia, blaNDM-1, clinically significant isolate, immunocompromised patient

Original Submission: 23 July 2017; Revised Submission: 26 September 2017; Accepted: 4 October 2017

Article published online: 16 October 2017

Corresponding author: M. Almuzara, Hospital Interzonal de Agudos Eva Perón, Laboratorio de Bacteriología, Av Dr Ricardo Balbin 3170, San Martín, Buenos Aires, 1650, Argentina E-mail: marisaalmuzara@gmail.com

Acinetobacter species are opportunistic pathogens that are responsible for nosocomial infections and outbreaks, especially in intensive care units. Most of the clinically significant isolates are resistant to a variety of antibiotics including carbapenems, which are the drug of choice to treat Acinetobacter infections.

In past years blaNDM-1 has increasingly been spread among Gram-negative bacteria and has been recognized as an important mechanism of carbapenem resistance in Acinetobacter baumannii and other species of this genus [1,2]. Several reports of Acinetobacter spp. harbouring blaNDM-1 have suggested that Acinetobacter could serve as a source and spread of this threatening carbapenemase.

Among the more frequent non-baumannii Acinetobacter species causing infections, we found A. junii, A. soli, A. ursingii, A. nosocomialis and A. lwofii [3–5]. However, A. schindleri, which was first described in isolates recovered mostly from nonsterile body sites of outpatients, has not been reported in clinically significant isolates from seriously ill hospitalized patients. A. schindleri harbouring blaNDM-1 recovered during routine groin surveillance from a patient with a blast injury during combat in Afghanistan was previously described [6]; however, the clinical significance of the present isolate was not mentioned.

Here we report the presence of a clinically significant A. schindleri (As190) blaNDM-1-positive strain isolated in a 52-year-old woman with a history of positive serology for HIV and hepatitis C virus. The patient also had a history of cocaine addiction, and she had been diagnosed with breast cancer and treated with chemotherapy and radiotherapy. Fifteen days before admission, she sought care for headache, disorientation, vomiting and weakness in the lower limbs. Computed tomographic scan of her brain revealed cystic lesion in the frontotemporal area, with a midline deviation and perilesional edema. She experienced marked deterioration of consciousness, requiring decompressive craniectomy. During surgery a sample of the cyst was taken for culture; the cultured sample grew Pseudomonas stutzeri. The microorganism was sensitive to cefepime, ceftazidime and carbapenems. After being treated with ceftazidime (2 g every 8 hours) for 4 weeks and then discharged with good clinical evolution, she was readmitted to hospital with sensorimotor deterioration, aspiration pneumonia and febrile syndrome. A new computed tomographic scan
revealed an increased cystic lesion, with increased oedema and midline deviation.

The patient was empirically treated with vancomycin and meropenem, and two blood cultures were performed. At 24 hours’ incubation, a Gram-negative bacillus (one of two samples) was isolated which was identified as *Pseudomonas fluorescens* by VITEK 2 (bioMérieux, Marcy l’Étoile, France) and then as *A. schindleri* by matrix-assisted desorption ionization—time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany). This identification was confirmed by rpoB gene sequencing (100% homology). Antimicrobial susceptibility testing was performed using VITEK 2, and the results were interpreted according to the 2017 guidelines of the Clinical and Laboratory Standards Institute (Table 1). In order to study the presence of metallo-β-lactamases (MBL), we used a double-disc assay using ethylenediaminetetraacetic acid (EDTA)-sodium mercaptoacetic disks (1900/750 μg (MBL), we used a double-disk assay using ethylenediaminetetraacetic acid (EDTA)-sodium mercaptoacetic disks (1900/750 μg). We obtained positive results only for the amplification of *bla* previously described primers to determine the presence of carbapenemase among this genus. The reactions were performed using the GoTaq enzyme according to the manufacturer’s instructions (Promega). We obtained positive results only for the amplification of blaNDM-1 in the As190 strain. Nucleotide sequencing and sequence analysis of the positive amplification product showed 99% identity with blaNDM-1. Considering the genes linked to blaNDM-1 [1,9], PCR reaction for ISAba125 and aphA6 were performed, giving positive results. Moreover, we performed PCR for other aminoglycoside genes, such as aac(6)-Ib, aacC2 and aphA1, and obtained negative results for all of them. To confirm the association among ISAba125, aphA6 and blaNDM-1, PCR reactions were performed. Positive PCR reactions were obtained for the following primer combinations: blaNDM-1 F-ISAba125F, blaNDM-1R-ISAba125F, blaNDM-1R-aphA6F, aphA6F-ISAba125F and aphA6F-ISAba125R. Sequence analysis confirmed the presence of aphA6-ISAba125-blaNDM-1 association.

In addition, conjugation assays were performed to see if blaNDM-1 could be transferred. Briefly, As190 and Escherichia coli J53-2 cells grown with agitation in Luria-Bertani broth were mixed (1:10 and 5:10 donor:recipient) and incubated for 18 hours at 30°C. Cells that may acquire NDM-1 were selected on Luria-Bertani agar with sodium azide (100 μg/mL) and ampicillin (100 μg/mL), and were incubated overnight at 37°C. Negative results were obtained, suggesting that blaNDM-1 is present in a nonconjugative element. To find out the exact location of the NDM-1, further studies need to be performed.

Carbapenemases are directly implicated in the increased rates of carbapenem resistance that have been observed lately. Carbapenem-resistant Gram-negative bacilli are of great concern because in some cases no treatment option is available. Continuous surveillance of carbapenem resistance, as well as correct identification at the species level, can contribute to the health system to combat bacterial infections. This report highlights the importance of *non-baumannii Acinetobacter* species harbouring blaNDM-1 and the broad dispersion of this carbapenemase among this genus.

### Acknowledgements

SM received a doctoral fellowship from Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). This work was supported by grants from the ‘Secretaría de Ciencia y Técnica de la Universidad de Buenos Aires’ (UBACyT) to CV and MSR, Buenos Aires, Argentina.

### Conflict of Interest

None declared.

### References

[1] Khan AU, Maryam L, Zarrilli R. Structure, genetics and worldwide spread of New Delhi metallo-β-lactamase (NDM): a threat to public health. BMC Microbiol 2017;17:101.
[2] Chatterjee S, Datta S, Roy S, Ramanan L, Saha A, Viswanathan R, et al. Carbapenem resistance in Acinetobacter baumannii and other Acinetobacter spp. causing neonatal sepsis: focus on NDM-1 and its linkage to ISAb1/25. Front Microbiol 2016;7:1126.

[3] Mittal S, Sharma M, Yadav A, Bala K, Chaudhary U. Acinetobacter lwofii an emerging pathogen in neonatal ICU. Infect Disord Drug Targets 2015;15:184–8.

[4] Wisplinghoff H, Paulus T, Lugenheim M, Stefanik D, Higgins PG, Edmond MB, et al. Nosocomial bloodstream infections due to Acinetobacter baumannii, Acinetobacter pittii and Acinetobacter nosocomialis in the United States. J Infect 2012;64:282–90.

[5] Romero-Gómez MP, Sundlov A, Sáez-Nieto JA, Alvarezc D, Peña P. Bacteremia due to Acinetobacter ursingii. Enferm Infec Microbiol Clin 2006;24:535–6.

[6] McGann P, Millillo M, Clifford RJ, Snesrud E, Stevenson L, Backlund MG, et al. Detection of New Delhi metallo-β-lactamase (encoded by blaNDM-1) in Acinetobacter schindleri during routine surveillance. J Clin Microbiol 2013;51:1942–4.

[7] Lee K, Lim YS, Yong D, Yum JH, Chong Y. Evaluation of the Hodge test and the imipenem-EDTA double-disk synergy test for differentiating metallo-beta-lactamase–producing isolates of Pseudomonas spp. and Acinetobacter spp. J Clin Microbiol 2003;41:4623–9.

[8] Pasteran F, Mora MM, Albornoz E, Faccone D, Franco R, Ortellado J, et al. Emergence of genetically unrelated NDM-1–producing Acinetobacter pittii strains in Paraguay. J Antimicrob Chemother 2014;69:2575–8.

[9] Fu Y, Du X, Ji J, Chen Y, Jiang Y, Yu Y. Epidemiological characteristics and genetic structure of blaNDM-1 in non-baumannii Acinetobacter spp. in China. J Antimicrob Chemother 2012;67:2114–22.