

## BRIEF COMMUNICATION

### KPC-PRODUCING *Serratia marcescens* IN A HOME-CARE PATIENT FROM RECIFE, BRAZIL

Emmily MARGATE(1), Vera MAGALHÃES(1), Lorena Cristina Corrêa FEHLBERG(2), Ana Cristina GALES(2) & Ana Catarina Souza LOPES(1)

#### SUMMARY

In this brief communication we describe the occurrence of a KPC-producing *Serratia marcescens* isolate in a home-care patient from Recife, Brazil. The  $bla_{KPC}$ ,  $bla_{SPM}$ ,  $bla_{IMP}$ ,  $bla_{VIM}$ ,  $bla_{OXA}$ ,  $bla_{CTX-M}$ ,  $bla_{SHV}$ ,  $bla_{TEM}$  and  $bla_{GES}$  genes were investigated by Polymerase Chain Reaction (PCR) and DNA sequencing. The isolate was positive for  $bla_{KPC-2}$  and  $bla_{TEM-1}$  and was resistant to aztreonam, cefepime, cefotaxime, imipenem, meropenem, gentamicin, ciprofloxacin and ceftazidime, and susceptible only to amikacin, tigecycline and gatifloxacin. This is the first report in Brazil of KPC-producing *S. marcescens* clinical isolate outside of a hospital environment. Caregivers should be alert for the presence of this isolate in the community setting.

**KEYWORDS:** *Serratia marcescens*; KPC-2 beta-lactamase; Carbapenemase; Multidrug-resistance.

#### INTRODUCTION

The emergence of *Klebsiella pneumoniae* carbapenemase (KPC)-producing gram-negative bacteria is worrisome due to inter or intraspecies plasmid-mediated transfer of the  $bla_{KPC}$  gene<sup>14</sup>. Furthermore, KPC-producing isolates are commonly multidrug-resistant, reducing therapeutic options. Since the first occurrence of KPC-producing *K. pneumoniae* in the United States<sup>18</sup>, this enzyme has been described in several countries and in different species, mostly from nosocomial infections<sup>2,3,8,11,13,16</sup>. Nevertheless, the spread of KPC-producing multidrug-resistant isolates in the community can also be a cause for great concern. In this study, we describe the emergence of the  $bla_{KPC-2}$  gene in *Serratia marcescens* isolated outside of a hospital environment in Brazil.

#### MATERIAL AND METHODS

One isolate of *Serratia marcescens* from the tracheal aspirate of a sixty-three-year-old male with amyotrophic lateral sclerosis, diagnosed at a private laboratory in Recife, Brazil, in September, 2010, was analyzed. The patient had been receiving medical attention at home since his last hospitalization in a private hospital, in July, 2010. The isolate was initially identified by biochemical tests and confirmed using MALDI-TOF mass spectrometry methodology (Bruker Daltonics, Germany).

Susceptibility testing was performed by the Etest (BioMérieux, Marcy l'Étoile, France) for aztreonam, cefepime, cefotaxime, ceftazidime, ciprofloxacin, gentamicin, imipenem and meropenem, and the disk diffusion method<sup>6</sup> for amikacin and gatifloxacin. Minimum inhibitory concentrations (MICs) were interpreted according to Clinical

and Laboratory Standards Institute (CLSI) guidelines. The modified Hodge test (MHT) with ertapenem disks (10 µg) was used for phenotypic detection of carbapenemase activity<sup>12</sup>.

Specific primers were used under standard PCR conditions to detect carbapenemase and ESBL encoding genes such as  $bla_{SPM}$ ,  $bla_{IMP}$ ,  $bla_{VIM}$ ,  $bla_{KPC}$ ,  $bla_{CTX-M}$ ,  $bla_{SHV}$ ,  $bla_{TEM}$ ,  $bla_{GES}$ ,  $bla_{OXA-48}$ <sup>15</sup>,  $bla_{OXA-23}$ ,  $bla_{OXA-24}$ , and  $bla_{OXA-58}$ <sup>17</sup>, followed by DNA sequencing (ABI 337 sequencer, Applied Biosystems, Foster City, CA). The nucleotide sequences were analyzed with software available at the National Center for Biotechnology Information website (<http://blast.ncbi.nlm.nih.gov/Blast.cgi>).

#### RESULTS AND DISCUSSION

The *Serratia marcescens* isolate was resistant to aztreonam (MIC, 128 µg/mL), cefepime (MIC, 64 µg/mL), cefotaxime (MIC, 128 µg/mL), ceftriaxone (MIC, > 32 µg/mL), imipenem and meropenem (MIC, > 32 µg/mL), gentamicin (MIC, >32 µg/mL) and ciprofloxacin (MIC, 4 µg/mL) and showed positive MHT results. On the other hand, the isolate was susceptible to amikacin and gatifloxacin, exhibiting reduced susceptibility to ceftazidime (MIC, 8 µg/mL). *S. marcescens* carried  $bla_{KPC-2}$  (GenBank accession number JX131687) and  $bla_{TEM-1}$  genes (GenBank accession number JX293719).

The spread of KPC has been frequently reported in Enterobacteriaceae, mainly in *K. pneumoniae*. In Brazil, the occurrence of KPC-producing *S. marcescens* isolates was reported by DEL PELOSO *et al.*<sup>7</sup> in intensive care unit (ICU) patients with urinary sepsis. Although the occurrence of  $bla_{KPC-2}$  in *S. marcescens* isolates has been described in nosocomial strains<sup>4,16</sup>, ICU

(1) Departamento de Medicina Tropical, Universidade Federal de Pernambuco, Recife, PE, Brazil.

(2) Laboratório alerta, Divisão de Doenças Infecciosas, Universidade Federal de São Paulo, São Paulo, SP, Brazil.

**Correspondence to:** Prof. Dr. Ana Catarina Souza Lopes, Phone 55 (81) 2126.8526. E-mail: ana.lopes.ufpe@gmail.com

patients may continue to be colonized by carbapenemase-producing isolates for long periods after hospital discharge, allowing its potential spread to households and the community<sup>9,10</sup>. In a study conducted by CHEN *et al.*<sup>5</sup> at a hospital in Virginia, USA, 58 patients with a mean age of 70 years were identified with infection or colonization by KPC-producing *K. pneumoniae*, 36% of whom were admitted from nursing homes or long-term care facilities (LTCF). The mean time to isolate a KPC-producing organism was 1.5 days after admission, suggesting that KPC-producing organisms were acquired in the community and that person-to-person transmission of KPC-producing organisms in the community is possible. GOTTESMAN *et al.*<sup>9</sup> described extra-hospital dissemination of a KPC-producing *K. pneumoniae* isolate in Israel, where a patient likely acquired the isolate from his wife, who had been previously hospitalized.

In the present study, the patient probably acquired the KPC-producing *S. marcescens* isolate during his previous hospitalization, since he received homecare after discharge. However, we want to emphasize the occurrence of the *bla*<sub>KPC</sub> gene outside the hospital environment, given that this resistance mechanism can easily spread among different species inside hospitals as well as in the community, as previously described<sup>9</sup>. The occurrence of KPC in community isolates of *K. pneumoniae* has only been reported in Brazil by ABOUD *et al.*<sup>1</sup>, in an outpatient from São Paulo.

The epidemiology of KPC-producing and multidrug-resistant organisms in a community setting remains poorly understood in Brazil. Thus, caregivers should be alert for the presence of this isolate, and prevention and control measures should be implemented not only in hospitals, but also in the community. The phenotypic and molecular characterization of community isolates can provide the essential data required to avoid the spread of this emerging resistance mechanism in the community.

## RESUMO

### ***Serratia marcescens* produtora de KPC em paciente sob assistência médica domiciliar em Recife, Brazil**

Nesse estudo descrevemos a ocorrência de um isolado de *Serratia marcescens* produtor de KPC em um paciente sob assistência médica domiciliar em Recife, Brazil. Os genes *bla*<sub>KPC</sub>, *bla*<sub>SPM</sub>, *bla*<sub>IMP</sub>, *bla*<sub>VIM</sub>, *bla*<sub>OXA</sub>, *bla*<sub>CTX-M</sub>, *bla*<sub>SHV</sub>, *bla*<sub>TEM</sub> and *bla*<sub>GES</sub> foram investigados pela Reação em Cadeia da Polimerase (PCR) e sequenciamento de DNA. O isolado foi positivo para os genes *bla*<sub>KPC-2</sub> and *bla*<sub>TEM-1</sub> e foi resistente a aztreonam, cefepime, cefotaxima, imipenem, meropenem, gentamicina, ciprofloxacina e ceftazidima, e susceptível apenas a ampicacina, tigeciclina e gatifloxacina. Este é o primeiro relato no Brasil de um isolado clínico de *S. marcescens* produtor de KPC fora de ambiente hospitalar. Os profissionais de saúde devem estar atentos à presença desse isolado na comunidade.

## REFERENCES

1. Abboud CS, Bergamasco MD, Doi AM, Zandonadi EC, Barbosa V, Cortez D, *et al.* First report of investigation into an outbreak due to carbapenemase-producing *Klebsiella pneumoniae* in a tertiary Brazilian hospital, with extension to a patient in the community. *J Infect Prev.* 2011;12:150-2.
2. Andrade LN, Curiao T, Ferreira JC, Longo JM, Clímaco EC, Martinez R, *et al.* Dissemination of *bla*<sub>KPC-2</sub> by the spread of *Klebsiella pneumoniae* clonal complex 258 clones (ST258, ST11, ST437) and plasmids (IncFII, IncN, IncL/M) among *Enterobacteriaceae* species in Brazil. *Antimicrob Agents Chemother.* 2011;55:3579-83.

3. Cabral AB, Melo RC, Maciel MA, Lopes AC. Multidrug resistance genes, including *bla*(KPC) and *bla*(CTX)-M-2, among *Klebsiella pneumoniae* isolated in Recife, Brazil. *Rev Soc Bras Med Trop.* 2012;45:572-8.
4. Cai JC, Zhou HW, Zhang R, Chen GX. Emergence of *Serratia marcescens*, *Klebsiella pneumoniae*, and *Escherichia coli* isolates possessing the plasmid-mediated carbapenem-hydrolyzing beta-lactamase KPC-2 in intensive care units of a Chinese hospital. *Antimicrob Agents Chemother.* 2008;52:2014-8.
5. Chen LF, Anderson DJ, Paterson DL. Overview of the epidemiology and the threat of *Klebsiella pneumoniae* carbapenemase (KPC) resistance. *Infect Drug Resist.* 2012;5:133-41.
6. CLSI. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twentieth Informational Supplement, M100-S20. Wayne: CLSI; 2010. p. 160.
7. Del Peloso PF, Barros MFL, Santos FA. Sepsis por *Serratia marcescens* KPC. *J Bras Patol Med Lab.* 2010;46:365-7.
8. Fehlberg LC, Carvalho AM, Campana EH, Gontijo-Filho PP, Gales AC. Emergence of *Klebsiella pneumoniae*-producing KPC-2 carbapenemase in Paraíba, Northeastern Brazil. *Braz J Infect Dis.* 2012;16:577-80.
9. Gottesman T, Agmon O, Shwartz O, Dan M. Household transmission of carbapenemase producing *Klebsiella pneumoniae*. *Emerg Infect Dis.* 2008;14:159-60.
10. Heseltine P. Has resistance spread to the community? *Clin Microbiol Infect.* 2000;6(Suppl 2):11-6.
11. Jácome PR, Alves LR, Cabral AB, Lopes AC, Maciel MA. First report of KPC-producing *Pseudomonas aeruginosa* in Brazil. *Antimicrob Agents Chemother.* 2012;56:4990.
12. Lee K, Chong Y, Shin HB, Kim YA, Yong D, Yum JH. Modified Hodge and EDTA-disk synergy tests to screen metallo-beta-lactamase-producing strains of *Pseudomonas aeruginosa* and *Acinetobacter* species. *Clin Microbiol Infect.* 2001;7:88-91.
13. Monteiro J, Santos AF, Asensi MD, Peirano G, Gales AC. First report of KPC-2-producing *Klebsiella pneumoniae* strains in Brazil. *Antimicrob Agents Chemother.* 2009;53:333-4.
14. Petrella S, Ziental-Gelus N, Mayer C, Renard M, Jarlier V, Sougakoff W. Genetic and structural insights into the dissemination potential of the extremely broad-spectrum class A  $\beta$ -lactamase KPC-2 identified in an *Escherichia coli* strain and an *Enterobacter cloacae* strain isolated from the same patient in France. *Antimicrob Agents Chemother.* 2011;52:3725-36.
15. Picão RC, Poirel L, Gales AC, Nordmann P. Diversity of beta-lactamases produced by ceftazidime-resistant *Pseudomonas aeruginosa* isolates causing bloodstream infections in Brazil. *Antimicrob Agents Chemother.* 2009;53:3908-13.
16. Tsakris A, Voulgari E, Poulou A, Kimouli M, Pournaras S, Ranellou K, *et al.* *In vivo* acquisition of a plasmid-mediated *bla*<sub>KPC-2</sub> gene among clonal isolates of *Serratia marcescens*. *J Clin Microbiol.* 2010;48:2546-9.
17. Woodford N, Ellington MJ, Coelho JM, Turton JF, Ward ME, Brown S, *et al.* Multiplex PCR for genes encoding prevalent OXA carbapenemases in *Acinetobacter* spp. *Int J Antimicrob Agents.* 2006;27:351-3.
18. Yigit H, Queenan AM, Anderson GJ, Domenech-Sanchez A, Biddle JW, Steward CD, *et al.* Novel carbapenem-hydrolyzing  $\beta$ -lactamase, KPC-1, from a carbapenem-resistant strain of *Klebsiella pneumoniae*. *Antimicrob Agents Chemother.* 2001;45:1151-61.

Received: 23 April 2014

Accepted: 11 November 2014