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Isolation of NDM-producing *Providencia rettgeri* in Brazil

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Sir,

New Delhi metallo-β-lactamase (NDM) was first identified in 2009 in a *Klebsiella pneumoniae* isolated from a patient in a Swedish hospital who had been previously hospitalized in India in 2008.[1] Since then, different bacterial species carrying the bla_{NDM} gene have been isolated, mostly in the Indian subcontinent, but also in several other countries around the world. Here, we report the first description (to our knowledge) of NDM-1 in Brazil.

In early 2013, a diabetic patient with peripheral vascular disease was admitted to a public hospital in southern Brazil (Rio Grande do Sul state) with a diabetic foot infection. Three weeks later, he was discharged from the hospital for ambulatory treatment with 500 mg of ciprofloxacin orally every 12 h. However, a month later he returned to the hospital with worsening of clinical signs and underwent toe amputation. Amoxicillin/clavulanate (1000/200 mg) intravenously every 8 h was initiated prior to surgery and maintained until patient discharge. A fragment of soft tissue from the toe sent for culture yielded growth of a carbapenem-resistant *Providencia rettgeri*, in which bla_{NDM-1} was detected. The patient recovered well and was discharged. Previous travel history to other countries was not established.

The identification of the isolate was confirmed by the API 20E system (bioMérieux, Marcy l'Étoile, France) and 16S rRNA gene sequencing. It was resistant to imipenem (MIC 4 mg/L) and susceptible to ertapenem (MIC 0.5 mg/L) and meropenem (MIC 0.75 mg/L) using Etest (AB bioMérieux, Solna, Sweden) according to CLSI 2013 breakpoints.[2] This resistance profile is very unusual in carbapenemase-producing bacteria. However, ertapenem susceptibility was also described in an NDM-producing *P. rettgeri* isolated from Israel.[3] Screening for carbapenemase/metallo-β-lactamase production yielded positive results with imipenem/EDTA,[4] but yielded negative results when using the modified Hodge test. PCR screening for β-lactamase genes (bla_{NDM}, bla_{KPC}, bla_{OXA-48}, bla_{VIM}, bla_{IMP}, bla_{CTX-M}, bla_{TEM}, bla_{SHV} and bla_{GES}) followed by DNA sequencing identified only the presence of bla_{NDM-1}.

Antimicrobial susceptibility profiling analysis performed with Etest indicated that the isolate displayed a multidrug resistance profile. According to CLSI 2013,[2] it was resistant to ceftazidime, cefotaxime and ciprofloxacin (MICs >256, 16 and >32 mg/L, respectively) and showed intermediate susceptibility to gentamicin (MIC 8 mg/L) and susceptibility to amikacin (MIC 3 mg/L). According to EUCAST breakpoints,[5] it was resistant to tigecycline (MIC 2 mg/L).

Infections due to multidrug-resistant carbapenemase-producing strains are commonly treated with polymyxin B and/or tigecycline. However, this isolate was intrinsically resistant to polymyxin B and presented intermediate susceptibility to tigecycline, creating a serious problem for the choice of therapy.

The presence of visible plasmid DNA in the *P. rettgeri* isolate was not observed using alkaline lysis methodology.[6] We also performed hybridization experiments to determine whether the bla_{NDM-1} gene was located in a low-copy plasmid (not detectable by ethidium bromide staining), but no hybridization was observed. These observations suggest that the bla_{NDM-1} gene in this strain is most likely chromosomally integrated.

To characterize the genetic structure surrounding the bla_{NDM-1} gene, a tagmentation library from genomic DNA was made with the Nextera XT DNA Sample Preparation Kit (Illumina) and pair-end sequenced on an Illumina Miseq system. Contigs obtained after *de novo* assembling the reads with Velvet algorithms[7] were

used for Blast searches against GenBank. A contig that carried the NDM gene was then used as a reference to map the reads and check contig assembly with Geneious 6.1.5 (Biomatters, New Zealand). By this approach, we observed that bla_{NDM-1} was located inside a composite transposon, named Tn*125* (10092 bp), the same as that described in NDM-1-producing *Acinetobacter baumannii* isolated from Germany.[8] Tn*125* is bracketed by two copies of the insertion sequence IS*Aba125*. In the *A. baumannii* isolate, Tn*125* was found on the chromosome, corroborating our results.

bla_{NDM-1} has been associated with different mobile elements; however, a complete form or variations of IS*Aba125* have been found upstream of the bla_{NDM-1} gene, suggesting that IS*Aba125* is responsible for mobilization of the gene. This insertion sequence has primarily been found in *A. baumannii*.[8]

In South America, the first description of NDM was in Uruguay in 2012, detected in the same species identified in our study (*P. rettgeri*).[9] The Rio Grande do Sul state (Brazil) and Uruguay border one another. However, to assert that Uruguay was the source of NDM, it would be necessary to perform molecular typing of the isolates to assess their clonality. The other reports of NDM in South America were of a *K. pneumoniae* outbreak in Colombia[10] and of *A. baumannii* in Paraguay,[9] other countries that border Brazil.

This first known detection of NDM in Brazil brings attention to the need for adopting effective measures to control the spread of this important carbapenemase in this country.

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Transparency declarations

None to declare.

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Rectal colonization with New Delhi metallo-β-lactamase-1-producing *Escherichia coli* prior to transrectal ultrasound (TRUS)-guided prostate biopsy

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Sir,

The global spread of New Delhi metallo-β-lactamase (NDM)-producing Enterobacteriaceae is of significant public health concern.[1] To date, NDM-producing Enterobacteriaceae have been isolated from numerous geographical regions, including Europe, North America, Australia and New Zealand.[1] In addition to hydrolysing carbapenems, NDM-producing organisms display resistance to a broad range of antimicrobial classes, primarily due to the presence of additional acquired plasmid-associated resistance genes.[2] As a result, infections caused by these organisms pose a considerable therapeutic challenge.

Transrectal ultrasound (TRUS)-guided prostate biopsy is a commonly performed urological outpatient procedure, with