Emergence of KPC-Producing *Pseudomonas aeruginosa* in the United States

Recent years have shown the emergence and dissemination of isolates of *Enterobacteriaceae* producing carbapenemases in different parts of the world (3). In many cases, those carbapenemases were KPC β-lactamases (5). Those enzymes hydrolyze all β-lactams, including carbapenems at a significant level, with the exception of cephemycins. The *bla*KPC-like genes have been reported most often from enterobacterial species (mostly Klebsiella pneumoniae species) recovered from several states in the United States (5). Besides the United States, KPC-producing *K. pneumoniae* isolates are found to be endemic in Greece and Israel, and there are, in addition, scattered reports from all over the world, including Western Europe, China, and South and Central America (5). In Colombia, the first identification of KPC-2-positive *Pseudomonas aeruginosa* isolates has been reported (6). We describe here the first identification of a KPC-producing *P. aeruginosa* isolate now in the United States.

In October 2009, a 68-year-old African-American man with a history of diabetes and hypertension was admitted with a myocardial infarction to a 1,500-bed teaching hospital in south Florida. Mechanical ventilation was required upon admission to the medical intensive care unit. He did not report any recent history of hospitalization or travel. The patient received an empirical antibiotic therapy consisting of ceftriaxone and vancomycin. Four weeks after admission, he developed hypothermia and blood and urine cultures grew *P. aeruginosa*. The patient subsequently received an empirical therapy based on meropenem. MICs of the *P. aeruginosa* P13 isolate measured by the Etest method (AB Biodisk, Solna, Sweden) and interpreted according to CLSI standards showed multidrug resistance including resistance to all carbapenems (carbapenem MICs of >256 μg/ml) (2). That isolate remained susceptible only to amikacin, gentamicin, and colistin. Consequently, the therapy was based on colistin and amikacin, and his subsequent blood cultures remained negative.

Molecular investigations were then performed on this isolate. PCR primers were used for the detection of Ambler class A and class B carbapenemases, followed by sequencing, which identified the *blaKPC-2* β-lactamase gene coding for carbapenemase KPC-2 (8). Analysis of the plasmid content of *P. aeruginosa* isolate 13 identified a single plasmid of ca. 66 kb that was successfully transferred to *Escherichia coli* by electroporation, with a selection performed on amoxicillin (100 μg/ml)-containing agar plates. The *E. coli* transformants expressing KPC-2 showed a 3-fold increase of MICs for imipenem, meropenem, and ertapenem, but they did not show any additional non-β-lactam resistance. PCR mapping performed as described previously (3) showed that the *blaKPC-2* gene was part of the *Tn4401b* transposon originally identified from a *K. pneumoniae* isolate from New York (4) and also identified from the clonally related Colombian *P. aeruginosa* isolates (6). Pulsed-field gel electrophoresis (PFGE) performed as described previously, however, indicated that *P. aeruginosa* isolate P13 was clonally unrelated to *P. aeruginosa* PA2404 from Colombia (data not shown).

This is the first identification of a KPC-producing *P. aeruginosa* isolate in the United States. It is noteworthy that it did not correspond to an imported case. It therefore remains to be evaluated to what extent KPC-type enzymes have spread in *P. aeruginosa* in the United States, since the phenotypic detection of production of that carbapenemase remains impossible. Use of molecular techniques may only allow determination of to what extent diffusion of such a *bla*KPC gene may contribute to the emergence of multidrug-resistant *P. aeruginosa* isolates in the United States. Taking in account the recent identification of KPC-positive *P. aeruginosa* isolates in South America and Caribbean islands (1, 7) and the importance of immigration from these countries to the United States, it is very likely that this resistance determinant has already spread widely.

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REFERENCES


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