Emergence in Italy of Klebsiella pneumoniae Sequence Type 258 Producing KPC-3 Carbapenemase

KPC-type carbapenemases are emerging resistance determinants in Klebsiella pneumoniae and other gram-negative pathogens, being an increasingly important mechanism of acquired resistance to carbapenems and other β-lactams (9, 10). KPC producers have recently undergone an important dissemination in the United States, Israel, and Greece and have been sporadically detected elsewhere in Europe, Latin America, and Asia (see references 1, 5, and 9 and references therein). Population analyses of KPC-producing K. pneumoniae isolates by multilocus sequence typing (MLST) have revealed the successful international spread of a sequence type (ST) 258 clone (1, 7, 12).

In this article, we report on the first detection of KPC-producing ST 258 K. pneumoniae in Italy.

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K. pneumoniae FIPP-1 was isolated in October 2008 from an inpatient with a complicated intra-abdominal infection at Florence University Hospital. FIPP-1 was resistant to carbapenems (MICs > 32 mg/liter) and other agents, except colistin, gentamicin, and tigecycline (Table 1). The infection was successfully treated with tigecycline following failure of an empirical carbapenem-based regimen.

Analysis of β-lactamase genes by PCR and sequencing revealed the presence of blaKPC-3, blaTEM-1, blaoXA-9, and blashv-11, while genes encoding other enzymes (CTX-M type, VIM type, and OXA-48) were not detected. MLST analysis (3) assigned FIPP-1 to ST 258. Sequencing of the ompK35 and ompK36 genes (6) showed that both genes were disrupted (by a G insertion at position 122 and by insertion of an IS5-like element, respectively), suggesting that a permeability defect contributed to the high carbapenem MICs of FIPP-1.

Transformants showing resistance or reduced susceptibility to all β-lactams (Table 1) were obtained by electroporation of Escherichia coli XL-1 blue with a plasmid preparation (11) from FIPP-1. Transformants yielded a positive PCR result for the blaKPC, blatem, and blaoXA-9 genes, suggesting that the three β-lactamase determinants were carried on the same plasmid, as previously observed (4).

PCR mapping and sequencing with primers KPC_istB_fw (5’-GCTACCCGTGGAAGGACAAG-3’) and KPC_tnpA_Rev (5’-GTCATGCGAAGACCCATCC-3’), targeting blaKPC-flanking sequences (4, 7, 8), showed that in FIPP-1, blakPC-3 was carried in a Tn4401a genetic context identical to that found in ST 258 blakPC-3-positive isolates from Israel but different from the Tn4401b context of blakPC-3-positive isolates from other countries (4, 7, 8).

Epidemiological analysis did not reveal any recent travel to settings of KPC endemicity. The only potential link with an area of endemicity was the presence of a training physician visiting from Israel, who had cared for the patient. The identity of ST and genetic context of FIPP-1 was confirmed with those of KPC-producing isolates from Israel (7, 12) support a similar origin. Pharyngeal and rectal swabs voluntarily provided by the trainee 2 months after the case report were negative for K. pneumoniae. However, this finding could not rule out colonization by a KPC-producing strain at the time of the patient’s care.

Carbapenem resistance in the Enterobacteriaceae is still very uncommon in Italy (http://www.earsr.rivm.nl). To the best of our knowledge, FIPP-1 is the first KPC-producing K. pneumoniae strain detected in Italy, a finding of major concern due to the high spreading propensity that KPC-positive K. pneumoniae of ST 258 has shown in other settings, with dramatic consequences for the epidemiology of antibiotic resistance. This report also underscores the potential role of the mobility of training health care personnel in the international dissemination of similar multidrug-resistant strains.

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