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A carbapenem-resistant *Klebsiella pneumoniae* isolate harboring KPC-1 from Italy

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SUMMARY

Carbapenem-resistant gram-negative pathogens represent an emerging threat to the management of hospital-acquired infections. Although the isolation of carbapenem-resistant enterobacteriaceae remains unusual, the frequency of carbapenemases producing *Klebsiella pneumoniae* is increasing in different geographic regions: the majority of isolates has been collected in the USA, but recently KPC-producing *K.pneumoniae* were reported from China, Israel, Greece, France, Norway and Sweden. We report a KPC1-producing *K. pneumoniae* isolate from Italy. This datum enlarges the geographical area where the KPC-producing *K.pneumoniae* strains are diffuse.

KEY WORDS: Klebsiella pneumoniae, Carbapenem resistance, KPC

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LETTERS

Carbapenems are widely used for the treatment of infections caused by multidrug resistant gram-negatives showing extended-spectrum beta-lactamase (ESbL) production. While carbapenem resistance has become quite common for *Pseudomomas aeruginosa* and *Acinetobacter baumannii*, it is still very rare among enterobacteriaceae. However, the frequency of carbapenem-resistant enterobacteriaceae is increasing in different geographic regions and represents an important threat to the management of hospital-acquired infections (Nordmann, 2009).

Carbapenem-hydrolyzing enzymes include metallo beta-lactamases, expanded-spectrum oxacillinases, or carbapenemases (KPC). The majority of KPC harboring enterobacteriaceae (mostly *Klebsiella pneumoniae*) have been collected in the northeastern USA (Wootford, 2004). Recently KPC-producing *K.pneumoniae* were reported from China, Israel, Greece, France, Norway and Sweden (Giakkoupi, 2009; Samuelsen, 2009).

We report a KPC-producing *K. pneumoniae* isolate from Italy. The strain was isolated in May 2009 from an 81-year-old woman with recurrent urinary tract infections (UTI). The patient was admitted to the San Giovanni in Persiceto Hospital near Bologna in January 2009 and then was transferred to a long-stay institution for the elderly in February.

From January to May she suffered several episodes of UTI. Two subsequent urine samples showed the growth of different pathogens: a methicillin-resistant *Staphylococcus aureus*, and an ESbL-producing *Escherichia coli*.

After the last result the woman was given i.v. meropenem (500 mg three times a day for 10 days). A third urine culture obtained 2 weeks after the end of the therapy disclosed a *K pneumoniae* isolate resistant to all beta-lactam antibiotics including meropenem, aminoglycosides, sulphonamides and fluoroquinolones (Table 1). Susceptibility testing was performed by Vitek2 and the results were further confirmed by Etest and disk diffusion assay. The modified Hodge test was used as phenotypic confirmatory test of KPC-production following the Clinical and Laboratory

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TABLE 1 - *MIC values of selected antimicrobial agents for the KPC1-harboring K. pneumoniae isolate.*

Antimicrobial agents	*MIC (mg/ml)*
Imipenem*	>32
Meropenem	>32
Ertapenem*	>32
Cefotaxime	16
Ceftazidime	>32
Cefoxitin	>64
Piperacillin/tazobactam	>128
Amoxicillin/clavulanic acid	>32
Amikacin	>64
Gentamicin	>16
Ciprofloxacin	>4
Sulfamethoxazole/trimethoprim	>302
Nitrofurantoin	>512

*MIC values were evaluated by using the Etest.

Standards Institute (CLSI) 2009 guidelines (CLSI, 2009).

The isolate showed MIC values >32 mg/ml for imipenem, meropenem and ertapenem. The modified Hodge test was clearly positive demonstrating the presence of KPC activity. The presence of bla_{TEM}, bla_{SHV} bla_{KPC-1} was investigated by PCR performed with specific primers (Rasheed, 1997; Yigit, 2001). KPC amplicons were cloned and sequenced. The sequences data were compared with those available in the GenBank (http://blast.ncbi.nlm.nih.gov/Blast.cgi) database showing the highest homology (98%) with the KPC-1 sequence (accession number: AF297554.1). In addition, PCR analysis disclosed the SHV encoding gene. Up to now the isolation of carbapenem-resistant enterobacteriaceae has been unusual in Europe. In particular, carbapenemases of the KPC type seem to be sporadically present in different countries, mainly in the Mediterranean region (Israel, Greece, France). To our knowledge any epidemiological link between the patient from whom the carbapenem-resistant *K. pneumoniae* was isolated and clinical settings where KPC-producing klebsiellae are known to be endemic is lacking. To date there are no published data on the identification of KPC-1 harboring *K.pneumoniae* isolates in Italy. This result enlarges the geographical area where the KPC-producing *K. pneumoniae* strains are diffuse.

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