Rapid communications

FIRST ISOLATIONS OF KPC-2-CARRYING ST258 KLEBSIELLA PNEUMONIAE STRAINS IN FINLAND, JUNE AND AUGUST 2009

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The first two *Klebsiella pneumoniae* carbapenemase-producing (KPC) type 2 strains carrying ST258 were detected in Finland in June and early August 2009. They were found colonising two patients transferred from the Mediterranean; one patient referred from a hospital in Greece where isolates were first found in 2007 and another from Italy where the first isolates have been described only very recently.

Case 1

The first carbapenemase-producing *Klebsiella pneumoniae* (KPC) strains in Finland were detected this summer in two patients transferred to Helsinki University Central Hospital (HUCH) from Crete, Greece, and northwestern Italy, respectively. Case 1 was a patient transferred from Greece at the end of June 2009. In Greece, the patient was initially hospitalised at a ward but later transferred to the intensive care unit, due to pneumonia and acute myocardial ischemia. The clinical history upon referral to our hospital did not mention antibiotic treatment although it is highly probable that antibiotics were used when the patient was first admitted to hospital in Greece.

Since the patient arrived to the HUCH intensive care unit from a high risk epidemic area where carbapenemase-carrying strains are common, a stool sample was tested for extended spectrum beta-lactamase (ESBL) and carbapenem resistance, using ESBL Chrom-ID agar (bioMérieux, Marseille, France) detecting both ESBLs and AmpC at the HUCH laboratory. *Klebsiella pneumoniae* grew on this plate; from this isolate, a direct KPC PCR was done, and sequencing of the PCR product confirmed the gene to be *bla*_{KPC-2}. Antibiotic susceptibility was tested using Etests (AB Biodisk, Solna, Sweden). The isolate was resistant or intermediately resistant to all antibiotics except trimethoprim-sulphamethoxazole and gentamicin (Table). Case 1 later died of multiorgan failure, not from infection related to the KPC strain.

Case 2

Case 2 was a patient transferred to Finland from north-western Italy in mid- August, after having been hospitalized for ten days during a trip due to seizures, unconsciousness and anaemia caused by an underlying alcohol-induced liver cirrhosis and total red cell aplasia. The clinical history upon referral to our hospital did not

mention antibiotic treatment, however, it is highly probable that antibiotics were used at the hospital in Italy. The patient was found to have a chronic sacral wound from which a swab was taken and analysed at the HUCS laboratory.

K. pneumoniae grew on the culture plate and the isolate was further analysed as it showed high level resistance to all β -lactams, including carbapenems. It remained susceptible only to colistin and gentamicin (Table). The isolate was found to be positive for *bla*_{KPC-2} by PCR and sequencing. Case 2 later died from the multiple underlying conditions unrelated to the KPC strain.

TABLE

Minimum inhibitory concentration (MIC) profiles of the carbapenem-producing *Klebsiella pneumoniae* isolates*, Finland, June-August 2009 (n=2)

Antibiotic	Case 1	Case 2
Piperacillin/tazobactam	>256	>256
Cefuroxime	>256	>256
Ceftazidime	>256	>256
Cefotaxime	>256	48
Aztreonam	>256	>256
Ertapenem	32	>32
Imipenem	8	>32
Meropenem	32	>32
Colistin	24	0.19
Doxicycline	6	6
Minocycline	4	3
Tigecycline	2	2
Amikacin	48	32
Gentamicin	2	2
Tobramycin	16	12
Trimethoprim/sulphamethoxazole	0.38	>32

*Both isolates were also resistant to levofloxacin, cefpodoxime, cefpodoxime/clavulanic acid, ceftazidime/clavulanic acid and cefotaxime/clavulanic acid, tested using Oxoid disks (Oxoid, Basingstoke, UK).

Results

The isolates were sent for multilocus sequence typing (MLST) and pulsed-field gel electrophoresis (PFGE) typing to the National Institute for Health and Welfare, where the PCR results were confirmed. Both strains contained *bla*_{TEM-1}, and pyrosequencing identified an ESBL variant of *bla*_{SHV} with Gly to Ser and Glu to Lys mutations at positions 238 and 240, respectively. PCR was negative for CTX-M, VIM-, IMP-, OXA-48 and GES-genes. Hydrolysis of imipenem was confirmed by spectrophotometric analysis of crude cell extracts. MLST [1] showed that both isolates belonged to the epidemic clone ST258. PFGE showed the strains to be somewhat similar (80%) to each other, as also found in other studies on this clone [2,3].

Conclusions

KPC-producing *Klebsiella pneumoniae* was first detected in North Carolina, USA, in 1996 [4]. After first only causing local epidemics on the east coast of the USA during the end of the 1990's and at the beginning of the new millennium [5,6], the KPC epidemic now seems to be accelerating [7].

Both Finnish isolates belonged to the clone ST258, which has been shown to account for probably 70% of the KPC-positive *K. pneumoniae* isolates sent to the US Centers for Disease Control and Prevention (CDC) [2]. It has also been found in Norway and Sweden in patients transferred from Greece and Israel in 2007 [3], in an outbreak strain in Israel [2] as well as in isolates in Poland [8] and Italy [9]. No doubt, MLST of KPC strains from around the world will find that many older isolates also belong to this clone. The resistance varies between isolates of this clone; gentamicin is the only antibiotic effective against all isolates. The Norwegian, Swedish and Polish isolates were reported to contain the beta-lactamase TEM-1 and ESBL beta-lactamases SHV-11 or -12, similarly to our strains, although we have not yet confirmed which SHV ESBL our strains contain.

The first Swedish and Norwegian cases were described at the end of 2007 [10,3]. The preparedness level in Finland was also increased at this time, by educating the clinical microbiology laboratories, and establishing reference methods.

Currently there is no compulsory screening programme for carbapenemase-producing pathogens at national level in Finland, but the authors would strongly recommend that patients transferred from abroad should be screened. Chromogenic ESBL-selective plates seem to be a fast, simple and presumably sensitive tool to detect carriers of multiresistant gram-negative bacteria for this purpose. In addition to ESBLs they detect KPC strains, and in our experience possibly also metallo-beta-lactamase-carrying strains. At least stool/rectal samples should be tested, preferably also swabs from the oropharynx and axillae [11].

Fortunately, the largest tertiary care hospital in Finland stayed alert to the threat of KPC colonised patients and was thus able to detect these two strains. The epidemic spread of carbapenemase-carrying strains from colonised patients is well-documented [12], and should be taken seriously.

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