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Abstract (poster session)

Reversion to susceptibility in carbapenem-resistant clinical isolate of Klebsiella pneumoniae ST258 producing KPC-3 in a kidney-transplant patient

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Objectives: We report the case of a kidney-transplant patient, suffering recurrent infections by carbapenem-resistant ST258 Klebsiella pneumoniae. During the combined tigecycline-phosphomycin therapy, the patient developed a sepsis sustained by a ST258 carbapenem-susceptible strain, which was successfully treated with meropenem. Complete sequencing of plasmid content of the two susceptible and resistant strains was investigated. Methods:DNA sequences of plasmids contained in the extremely drug-resistant K. pneumoniae ST258 strain, producing the KPC-3 carbapenemase (LS6) and in the carbapenem susceptible (SC29) strain isolated from the same patient were obtained by applying the 454-GS FLX procedure. Results: The carbapenem resistant LS6 strain contained four plasmids: two IncF plasmids (pKPQIL-LS6, pKPN-LS6), one IncA/C (A/C-LS6) and one small ColE-like (col-LS6) for a total of 500 kb of plasmid DNA, encoding 24 resistance genes and two putative virulence clusters. pKpQIL-LS6 conferred carbapenem resistance by the presence of the blaKPC-3 gene. The pKPN-LS6 plasmid, conferred resistance to arsenic, copper, silver, chloramphenicol, macrolides, trimethoprim and streptomycin. pKPN-LS6 also encoded a Fec iron(III) dicitrate transport system, likely involved in the capacity of the bacterium to acquire iron in the human host, and a completely novel unknown region highly related to the Salmonella enterica phage epsilon 15. A/C-LS6, similarly to other IncA/C plasmids, encoded the CMY-6. The ColE-LS6 plasmid conferred gentamicin resistance. Three plasmids were identified in the carbapenem-susceptible SC29 strain: pKPN-SC29 and A/C-SC29 were identical to pKPN-LS6 and AC-LS6, respectively. The 48 kb pKpQIL-SC29 was a derivative of the pKpQIL-LS6 plasmid, showing a deletion of the entire Tn4401::blaKPC-3 transposon. The deletion also involved the entire tra locus and the antibiotic resistance region except the mer locus. This deletion was likely caused by an IS26-mediated looping out, consequent to the IS26-mediated integration of the ColE-plasmid within the pKpQIL-SC26 backbone. Conclusions: The loss of the carbapenem resistance determinant from the plasmid allowed a change in patient therapy, permitting the successful treatment with carbapenems. This report suggests that resistance determinants on plasmids that are not under positive selection may be unstable, allowing rearrangements that in our case played in favor of the loss of the carbapenem resistance.