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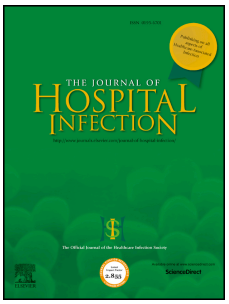

Mother-to-child transmission of KPC-producing *Klebsiella pneumoniae*: potential relevance of a low microbial urinary load for screening purposes

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Mother-to-child transmission of KPC-producing *Klebsiella pneumoniae*: potential relevance of a low microbial urinary load for screening purposes

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Sir,

In a previous report, we described the first case of a mother-to-child transmission of KPC carbapenemase-producing *Klebsiella pneumoniae* (KPC-KP) at birth, in an extremely low birth weight infant who developed sepsis caused by KPC-KP during the first week. The case was followed by a small outbreak of KPC-KP in the neonatal intensive care unit, which was controlled by the implementation of strict infection control measures [1]. Here we describe a new case of mother-to-child transmission of KPC-KP (involving two twins), that highlights the potential relevance of low urinary microbial loads in pregnancy for screening purposes.

The mother was a 32-weeks pregnant Italian citizen, admitted to the A. Manzoni Hospital of Lecco (Northern Italy) for preterm premature rupture of membranes. The clinical conditions were good, with no fever or signs of sepsis. No risk factors for MDR organisms were known. Ampicillin (2 g every 6 hours) and clarithromycin (500 mg every 12 hours) were given for 6 days, in accordance with the guidelines for the management of women with preterm premature rupture of membranes [2].

Three days after admission a surveillance urine culture yielded a *K. pneumoniae* at very low microbial load (≈1,000 CFU/ml). Despite the microbial load was below the significance level for uncomplicated urinary tract infection in pregnant women [3], the isolate was further investigated as part of an ongoing study protocol on carbapenem-resistant urinary tract isolates of Enterobacteriaceae. Antimicrobial susceptibility testing, carried out by broth microdilution (CLSI) and interpreted according to the 7.1 EUCAST clinical breakpoints (www.eucast.org), revealed that the isolate was resistant to extended-spectrum cephalosporins, carbapenems, and fluoroquinolones, and susceptible to aminoglycosides (amikacin and gentamicin), colistin, tigecycline, trimethoprim/sulfamethoxazole, and ceftazidime-avibactam (Table I). Rapid molecular analysis by the GeneXpert system (Xpert Carba-R, Cepheid, Sunnivale, CA) yielded a positive result for KPC carbapenemase gene, that was immediately communicated to clinicians. KPC-KP was subsequently isolated also from a rectal swab of the mother, and from the amniotic fluid collected at delivery (11 days after admission), while the routine culture from the placenta specimen (collected at birth) was negative.

At birth, the infants had a low weight (1756 g and 1780 g, respectively) but were in overall good clinical conditions. Microbiological screening, performed by throat and auricular swabs, taken after delivery, yielded negative results for KPC-KP. However, subsequent cultures of throat and rectal swabs from twin #1 (taken three days after delivery in both cases), and of conjunctival and rectal swabs from twin #2 (taken six and 13 days after delivery, respectively), resulted positive for KPC-KP. Since no signs of infection was present, no antimicrobial treatment was given to the infants, and the presence of KPC-KP was regarded as a colonization event. Both children were discharged after 24 days in good clinical conditions (twin #1, 2245 g; twin #2, 2330 g).

Further molecular analysis of the KPC-KP isolates (LC-1296/16, LC-1315/16, LC-1354/16, and LC1312/16), carried out by whole genome sequencing (HiSeq Illumina platform, Illumina, San Diego, CA, USA) revealed that all the isolates belonged to the same sequence type (ST) 307 and that all carried the same pattern of acquired resistance genes (including the $bla_{\text{KPC-3}}$ and $bla_{\text{SHV-28}}$ beta-lactamases) (Table I). Core genome SNP analysis, carried out using the CSI Phylogeny tool (https://cge.cbs.dtu.dk/services/CSIPhylogeny), demonstrated that the isolates were closely related to each other (SNPs differences range: 0-2) (Table II). These data confirmed that the strains from the mother and those from the two twins were the same.

Despite the absence of signs and symptoms of infection, screening and treatment of asymptomatic bacteriuria in pregnancy is currently a commonly recommended practice in several countries. However, only microbial loads of at least 10^5 CFU/ml are considered significant and reported by the laboratory [3, 4].

To the best of our knowledge, this is the first report that demonstrates the importance of taking into account a low microbial load of KPC-KP from urine samples in pregnancy as a risk factor for the mother-to child transmission of KPC-KP at birth. In our case, prompt communication of KPC-KP positivity enabled the maternity unit to rapidly implement strict infection control measures and limit hospital transmission. In fact, the mother, and subsequently the infants, were subjected to isolation regimen during hospitalization, and a dedicated staff was assigned to their care. In particular, the two infants were located in different boxes separated from other newborns, with a larger spacing between cots. Other measures such as improvement of hand hygiene compliance and deep cleaning of environment and equipment were adopted. No additional cases of KPC-KP

cross-transmissions were detected in the maternity unit. Based on this experience, screening of urine samples for resistant pathogens, even if at low load (below the clinical significance level), could be important in preventing their spread in the maternity units.

Conflict of interest statement

None declared.

Funding sources

None.

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Table I. Susceptibility profile of KPC-producing *Klebsiella pneumoniae* isolates

Patient	Code	Source	ST	Acquired resistance determinants	MIC values (S, I, R)* of various antimicrobial agents														
					AC	AZ	PT	CZ	CT	FP	ET	IM	MR	AK	GN	CI	TG	CO	ST	CZA
Mother	LC-1296/16	Urine	307	bla_{KPC-3}; bla_{SHV-28}; *strAB*	>32/2 (R)	64 (R)	64 (R)	>16 (R)	>4 (R)	8 (R)	>4 (R)	8 (I)	8 (I)	0.5 (S)	<=0,5 (S)	4 (R)	0.5 (S)	0.5 (S)	<=0,5/9,5 (S)	0.5 (S)
Twin #1	LC-1315/16	Rectal swab	307	bla_{KPC-3}; bla_{SHV-28}; *strAB*	>32/2 (R)	>64 (R)	>64 (R)	>16 (R)	>4 (R)	>8 (R)	>4 (R)	8 (I)	>8 (R)	0.5 (S)	<=0,5 (S)	4 (R)	0.5 (S)	0.5 (S)	<=0,5/9,5 (S)	0.5 (S)
Twin #2	LC-1354/16	Rectal swab	307	bla_{KPC-3}; bla_{SHV-28}; *strAB*	>32/2 (R)	>64 (R)	64 (R)	>16 (R)	>4 (R)	>8 (R)	>4 (R)	8 (I)	>8 (R)	0.5 (S)	<=0,5 (S)	4 (R)	0.5 (S)	0.5 (S)	<=0,5/9,5 (S)	2 (S)
Mother	LC-1312/16	Amniotic fluid	307	bla_{KPC-3}; bla_{SHV-28}; *strAB*	>32/2 (R)	>64 (R)	64 (R)	>16 (R)	>4 (R)	>8 (R)	>4 (R)	8 (I)	8 (R)	4 (S)	<=0,5 (S)	4 (R)	0.5 (S)	0.5 (S)	<=0,5/9,5 (S)	2 (S)

*MIC values indicate minimal inhibitory concentrations, as obtained by standard broth microdilution method. Interpretation based on current EUCAST criteria (http://www.eucast.org).

Abbreviations: AC, amoxicillin-clavulanate; AK, amikacin; AZ, aztreonam; CZ, ceftazidime; CZA, ceftazidime-avibactam; CI, ciprofloxacin; CO, colistin; CT, cefotaxime; ET, ertapenem; FP, cefepime; GN, gentamicin; IM, imipenem; MR, meropenem; PT, piperacillin-tazobactam; ST, trimethoprim–sulfamethoxazole; S, susceptible; I, intermediate; R, resistant.

Table II. Characteristics of *Klebsiella pneumoniae* isolates typed by whole genome sequencing.

Patient	**Code**	**Core genome SNPs[#]**				**Contigs (n)**	**N50 (bp)**	**L50 (n)**	**Total length (bp)**
		LC-1296/16	LC1312/16	LC-1315/16	LC-1354/16				
Mother	LC-1296/16	0	1	1	1	76	203258	9	5423722
Mother	LC1312/16	1	0	2	0	58	288790	6	5430120
Twin #1	LC-1315/16	1	2	0	2	69	203549	7	5429132
Twin #2	LC-1354/16	1	0	2	0	69	307600	6	5433433

[#]The core genome SNPs analysis was performed using the ST307 *K. pneumoniae* strain KPN11 (Acc. no. NZ_NCTN00000000.0) as reference.