Isolation of NDM-1-producing *Klebsiella pnemoniae* in Ireland, July 2011

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We report the identification of New Delhi metallo-beta-lactamase 1 (NDM-1)-producing *Klebsiella pnemoniae* in Ireland. The organism was resistant to multiple antibiotic classes, including carbapenems, and PCR and sequencing confirmed the presence of the bla_{NDM-1} gene, carried on a 98kb plasmid. The organism was isolated from an infant, who was born in India and moved to Ireland at the age of four months. This is the first reported isolation of an NDM-1-producing *Enterobacteriaceae* strain in Ireland.

Case report

A six-month old infant presented to the family doctor in May 2011 with a non-specific febrile illness. The child had been born in Kolkata, eastern India, by uncomplicated full-term vaginal delivery. The mother and child spent three to four days in hospital after the birth. The family (two parents and child) moved to Ireland when the child was four months old. The child, who had no underlying illness or past medical history of note, was treated empirically with amoxicillin/clavulanic acid for a suspected urinary tract infection shortly after arrival in Ireland; however, no urine sample was submitted for testing at this time. Six weeks later, the child presented again with a low-grade fever. A urine sample showed a white cell count of 1,700/mm^3 and greater than 10^5 bacteria/ml on culture. The isolate was identified as *Klebsiella pneumoniae* on VITEK 2 (bioMérieux, United States). It was resistant to meropenem (minimum inhibitory concentration (MIC) >16 mg/L), but susceptible to ciprofloxacin. After treatment with a 10-day course of ciprofloxacin, there was a good clinical response. A repeat urine sample after completion of ciprofloxacin therapy grew more than 10^5 bacteria/ml of an isolate identified as *Escherichia coli* resistant to ciprofloxacin, cefotaxime and cefoxitin but susceptible to ertapenem and trimethoprim. The child received a five-day course of trimethoprim and remains clinically well. A renal ultrasound was normal.

A rectal swab from the child, taken two weeks after the initial positive urine sample, yielded multiple isolates of *K. pneumoniae* including both carbapenem-resistant and carbapenem-susceptible but extended-spectrum cephalosporin-resistant isolates.

The case was investigated by the local Department of Public Health in accordance with international protocols [1]. Family screening for carriage of the NDM-1-producing strain was carried out on both urine and rectal samples of the parents. *E. coli* with a similar susceptibility pattern to the second urinary isolate from the child was isolated from rectal swabs from the parents, but carbapenem-resistant *K. pneumoniae* was not detected.

Laboratory characterisation

The carbapenem-resistant *K. pneumoniae* isolate from the initial positive urine sample (isolate number 2661) was referred to the Antimicrobial Resistance and Microbial Ecology Group at the National University of Ireland, Galway, for further characterisation. Meropenem and ertapenem MICs were both >32 µg/ml as determined by Etest. The full susceptibility profile, as determined by the Clinical and Laboratory Standards Institute (CLSI) disk diffusion method [2], is shown in the Table. The isolate was confirmed as a carbapenemase producer by the modified Hodge test of the CLSI, and metallo-beta-lactamase activity was indicated by a commercial synergy test (Rosco Diagnostica, Denmark). PCR and sequencing confirmed the presence of bla_{NDM-1}, and plasmid analysis revealed this was carried on a 98kb plasmid (data not shown) [3,4]. PFGE analysis using *Xba*I was carried out on two *K. pneumoniae* isolates from the child (the carbapenem-resistant *K. pneumoniae* and a carbapenem-sensitive *K. pneumoniae* rectal swab isolate) and on *E. coli* isolated from the child and from both parents [5]. The PFGE profiles of the two *K. pneumoniae* isolates from the child were not similar (data not shown). PFGE profiles of the three *E. coli* isolates were indistinguishable (one from each of the parents and one from the child).

Discussion

Infections caused by carbapenem-resistant *Enterobacteriaceae* isolates have been reported in

hospital outbreaks in Ireland [6], but isolates producing NDM-1 have not previously been identified in Ireland.

Carbapenemase-producing *Enterobacteriaceae* represent a major threat to current approaches to treatment of life-threatening *Enterobacteriaceae* infection. In addition to resistance to almost all available beta-lactam agents, many strains are frequently resistant to multiple classes of antimicrobial agents, including aminoglycosides and fluoroquinolones.

NDM-1-producing *K. pneumoniae* was first recognised in a Swedish patient in 2008 who was repatriated to Sweden from the Indian subcontinent [7]. Since then, NDM-1-producing isolates have been identified in patients in the United Kingdom who had a history of receiving healthcare in India and Pakistan [8]. The majority of reported clinical cases related to NDM-1-producing isolates to date have been in adults. However, NDM-1-producing *E. coli* has recently been reported from rectal screens of neonates returning to France after having attended healthcare facilities in Egypt and India [9]. Two cases of neonatal sepsis associated with NDM-1-positive *K. pneumoniae* have been reported from a neonatal intensive care unit in a tertiary referral hospital in Kolkata, India [10].

The source of colonisation/infection with NDM-1-producing *K. pnemoniae* in the child reported here cannot be established unequivocally. However, the fact that the child was born and lived the first few months in India, including a stay of a few days in hospital after birth, is likely to be of relevance given the reported high levels of carbapenemase-producing *Enterobacteriaceae* in India [11]. Although such organisms were not detected in either parent, a single rectal swab may not identify carriage, particularly if the organism is present in small numbers [12], and the parents may therefore potentially be colonised.

This case highlights the importance of testing isolates from routine clinical samples for susceptibility to carbapenem even in low-incidence areas to maximise the likelihood of detection of carbapenem-resistant *Enterobacteriaceae*, in order to guide therapy and prevent onward spread through implementation of transmission-based precautions and enhanced environmental cleaning (as was done in this case). Early recognition and reporting in low-incidence areas also provides an opportunity to establish national measures to prevent such isolates becoming endemic in healthcare settings. This report also highlights the importance of considering the possibility of carbapenem-resistant isolates in people returning from the Indian subcontinent.

Table

Susceptibility profile of NDM-1-producing *Klebsiella pneumoniae* urinary isolate recovered in Ireland, July 2011

Antibiotic	Susceptibility
Chloramphenicol	S
Minocycline	S
Tetracycline	S
Ciprofloxacin	S
Amikacin	R
Kanamycin	R
Ampicillin	R
Ceftazidime	R
Cefotaxime	R
Cefpodoxime	R
Cefoxitin	R
Aztreonam	R
Amoxicillin/clavulanic acid	R
Piperacillin/tazobactam	R
Sulphonamides	R
Streptomycin	R
Gentamicin	R
Nalidixic acid	R
Trimethoprim	R

NDM-1: New Delhi metallo-beta-lactamase 1; R: resistant; S: sensitive.

Susceptibility was determined by the Clinical and Laboratory Standards Institute (CLSI) disk diffusion method [2].

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