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Isolation of *Klebsiella pneumoniae* Producing NDM-1 Metallo-β-Lactamase from the Urine of an Outpatient Baby Boy Receiving Antibiotic Prophylaxis

New Delhi metallo-β-lactamase 1 (NDM-1) is a newly described metallo-β-lactamase (MBL) first identified in 2008 in single isolates of *Klebsiella pneumoniae* and *Escherichia coli*, with both recovered from a patient repatriated to Sweden after treatment in a hospital in New Delhi, India (8). Urinary tract infection (UTI) is a very common illness in children (4).

The first patient in Serbia with NDM-1-producing *K. pneumoniae* was a 7-month-old male baby. At the age of 4 months (in April 2011), he was hospitalized in Belgrade for prolonged constipation and suspected megacolon. On examination, the patient was afebrile, and laboratory studies including complete blood indices were normal. During the hospitalization, 10×10^3 CFU/ml *E. coli*, susceptible to antibiotics, was isolated from urine in the absence of leukocyturia. The patient was treated with cephalexin.

In June 2011, a voiding cystourethrogram revealed bilateral vesicoureteral reflux grade II. The patient was afebrile, laboratory studies including C-reactive protein were normal, and there was no leukocyturia. The patient was treated with amoxicillin/clavulanate (50 mg/kg of body weight/day divided every 8 h [q8h]) for 7 days, followed by cephalexin (10 mg/kg as a single daily dose) as an antibiotic prophylactic. In August 2011, 5×10^3 CFU/ml *K. pneumoniae*, named IT977, was isolated from urine. The isolate was resistant (disk diffusion test and Vitek 2) to ampicillin, ampicillin-sulbactam, piperacillin-tazobactam, cefazolin, ceftriaxone, cefepime, aztreonam, ertapenem, imipenem, meropenem, gentamicin, tobramycin, ciprofloxacin, moxifloxacin, nitrofurantoin, and trimethoprim-sulfamethoxazole, was susceptible to tigecycline and fosfomycin, and had intermediate susceptibility to amikacin according to the CLSI guidelines (2). A phenotypic confirmatory disk diffusion test using both cefotaxime and ceftazidime, alone and in combination with clavulanic acid, was negative for extended-spectrum β-lactamase production (2). This isolate was susceptible to colistin (MIC = 0.5 μg/ml; Etest).

The isolate was positive for MBL production in the imipenem-EDTA, ceftazidime-EDTA, and cefepime-EDTA combined disk tests. The gene bla_{NDM-1} was detected using PCR as described previously (5). In order to reveal the bla_{NDM-1} gene sequence, a cosmid library of *K. pneumoniae* IT977 total DNA (PstI digested) was constructed (5). Sequencing revealed the presence of the bla_{NDM-1} gene located on a 1,059-bp EcoRI fragment (GenBank accession no. HE866523).

To our knowledge, this is the first documented isolation of *Enterobacteriaceae* producing NDM-1 in Serbia. Reports of *Enterobacteriaceae* producing NDM-1 in patients who traveled in or originated from Serbia suggest that the Balkans may represent a second reservoir of NDM-1-producing bacteria (6, 7). Jovcic et al. reported isolation of a *Pseudomonas aeruginosa* strain producing NDM-1 in patients in the Military Medical Academy, Belgrade, Serbia (5). We did not investigate the other possible mechanisms of resistance to beta-lactam antibiotics in this isolate.

Our patient had no evidence of UTI, and the voiding cystourethrogram revealed bilateral vesicoureteral reflux grade II. He has never had leukocyturia or clinical signs or symptoms of infection, yet he was treated with antibiotics and prescribed antibiotic prophylactics. Some authors found that antimicrobial prophylaxis is associated with an increased risk of resistant infections (1, 3). With *Enterobacteriaceae* acquiring such powerful mechanisms of resistance, there is a need for additional critical review of antibiotic prophylaxis in children such as our patient.

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